THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

JANUARY, 1903.

SARCOMA OF THE THIRD CERVICAL SEGMENT: OPERATION; REMOVAL; CONTINUED IMPROVEMENT.[1]

By James W. Putnam, M.D.,

PROFESSOR OF NERVOUS DISEASES, MEDICAL DEPARTMENT, UNIVERSITY OF BUFFALO; CONSULTING NEUROLOGIST, BUFFALO GENERAL HOSPITAL,

AND

William C. Krauss, M.D.,

CONSULTING NEUROLOGIST, BUFFALO GENERAL HOSPITAL.

WITH A SURGICAL REPORT

By Roswell Park, A.M., M.D., LL.D.,

PROFESSOR OF SURGERY, MEDICAL DEPARTMENT, UNIVERSITY OF BUFFALO; SURGEON TO THE BUFFALO GENERAL HOSPITAL.

The literature on spinal cord tumors with operation begins with the epoch-making case of Horsley and Gowers in 1888, although Leyden in 1874 and Erb again in 1878 urged surgical procedure in cases where the diagnosis could be safely established. The high standing of the English neurologist, Sir William Gowers,[2] an honorary member of the Association; the accuracy of the diagnosis; the keenness and certainty of the surgeon's skill, and the brilliancy of the results obtained in this first operation attracted others to this most important field, so that Starr,[3] in June, 1895, was able to collect 22 cases of spinal cord tumors, with operations. Of these 22 the tumor was successfully removed in 13, while death followed the operation in 9. Of the successful operations, a recovery from the condition of paraplegia occurred

[1] Read at the Twenty-eighth Annual Meeting of the American Neurological Association held at New York, June 5, 6, and 7, 1902.

[2] Med. Chirurg. Trans., 1888, p. 407.

[3] The American Journal of the Medical Sciences, June, 1895, p. 613.

in 6. In explanation of the unfavorable results, Starr well says that an operation has not been undertaken until the tumor has been going on for a number of months, and until the secondary destruction of the spinal cord tissues was of such a nature that a regeneration of the nerve elements was practically out of the question.

Bruns, in 1898, collected 20 unquestioned cases of spinal tumor, with operation. In 18 of the 20 cases the correctly diagnosed tumor was removed during the operation; in 1 instance it was not found because the opening was made too low, and in another case because it was a flat sarcoma of the meninges, which was not recognized during the operation. In 6 of these 20 cases marked improvement and even recovery was attained—that is, exactly 30 per cent.; in 2 only very slight and in 1 temporary improvement followed. In 12 cases death occurred—9 soon after operation, by shock after hemorrhage and sepsis; 3 at a later date, by relapse, marasmus, and extension of the tumor, which was not discovered during the operation.

Of these 20 cases, in 14 the tumor was located in the thoracic region, 2 in the lumbar, 2 in the sacral, and 1 in the cervical. The nature of the tumor removed was sarcoma in 9, psammoma in 2, and 1 each of fibromyxoma, lipoma, endothelioma, echinococcus, lymphangioma, tubercle, and in 3 not stated. The tumor was found to be extradural in 11 cases, intradural in 7, and not stated in 2.

The next notable addition to the literature on the subject was made by Putnam and Warren,[1] of Boston, in 1899. They reported 33 cases of tumor with operation. Of these 7 led to recovery and 10 to more or less improvement, although only in 5 of these latter was the improvement considerable or lasting. The neoplasms removed in the satisfactory cases were fibroma in 3 cases, echinococcus in 2, and 1 each of lipoma, psammoma, and sarcoma.

In 10, perhaps 12 cases, operation seems to have hastened death, while in 9 the operation seems to have made little difference in the progress of the case. The location of the tumor in these cases was: extradural, 20; intradural, 7; intradural and extradural, 1; intramedullary, 1; not stated, 4. The nature of the tumor was sarcoma in 14, echinococcus in 5, fibroma in 2, psammoma in 2, and 1 each of endothelioma, cancer, fibromyxoma, chondrosarcoma, lipoma, lymphangioma, and tumor of the vertebra. The tumor was located in the thoracic region in 25 cases, 2 in the lumbar region, 1 in the sacral, 1 in the cervical, 1 in the thoracic and lumbar, 1 in lumbar and sacral, and 2 not stated.

The next classified list of spinal cord tumors with operation to appear in the current literature is that of Samuel Lloyd's, published in the

[1] The American Journal of the Medical Sciences, October, 1899.

Philadelphia Medical Journal, February 22, 1902. The list is incomplete, as it does not contain the case of Starr and McCosh,[1] published in the *Journal of the American Medical Association*, August 31, 1901; nor Oppenheim's case, published in the *Berliner klinische Wochenschrift*, January 13, 1902; nor Fedor Krause's case, published in the *Berliner klinische Wochenschrift*, June 3, 1901. The list includes some cases not properly belonging to spinal cord tumors.

Lloyd included 51 cases in his list. Of these 16 recovered, or 31.37 per cent.; 4 improved, 2 were unimproved, and 5 died immediately and 23 some time after the operation.

The location of the tumor was as follows: extradural, 29; intradural, 10; intravertebral, 10; extravertebral, 14; not stated, 3. The nature of the tumor was sarcoma in 15 cases, echinococcus in 8, lipoma in 3; cancer, abscess, fibroma, lymphangioma, psammoma in 2 each; myxosarcoma, myxoma, chondrosarcoma, osteosarcoma, enchondroma in 1 each, and in 10 not stated. The tumor was located 37 times in the thoracic region, 7 in the lumbar, 2 in the cervical, 1 in the sacral, and not stated in 2.

From a study of these different collections the sarcoma is by far the most common tumor affecting the spinal cord. It was found present in 45 per cent. in Bruns', 42 per cent. in Putnam's, and in 29.4 per cent. of Lloyd's cases. The most frequented portion seems to be the thoracic region, while the cervical is the least frequented. In situation the extradural is much more prevalent than the intradural, while the intramedullary is extremely rare.

The percentage of recovery in Bruns' and Lloyd's collection is practically the same, being 30 per cent. in the former and 31.37 per cent. in the latter. In Putnam and Warren's collection the percentage is lower, being 21.2 per cent., while the percentage of improvement is also 21.2 per cent. The history of the case which we desire to place on record is as follows:

April 2, 1902, Dr. Putnam was called to see the patient, J. E., and obtained the following history: Male, aged forty-five years; married, but has no children; habits temperate. Previous history of good health all his life and freedom from any serious accidents; no falls upon the back. In the autumn of 1900 he complained of occasional sudden, sharp attacks of pain. These would begin in the back of the neck and radiate around the neck and up the occiput. The pains would last from two to five minutes, during which time he says he suffered most intense agony. He would grasp a chair in front of him and hang on, but, in spite of himself, he would be forced to yell and scream with pain. He says that on two occasions he lost consciousness, and he would frequently have dizzy attacks. During the first few months the intervals of freedom from pain were often a week, but

[1] Starr, M. Allen. Philadelphia Medical Journal, February 8, 1902.

gradually the intervals shortened, until he would have them several times daily. In addition to the symptoms of periodical pain he suffered from some constipation and from difficulty in fully emptying the bladder. In the spring of 1901 he went to California, and later to Hot Springs, Ark., believing that he was suffering from rheumatism. His best recollection is that he had a sensation of numbness in the left hand in the spring of 1901, and that was followed by weakness of the muscles of the left hand and arm. The right hand was affected with numbness and weakness some months later. The legs were affected with weakness and disturbed sensation in December, 1901; he was, however, able to walk until the early part of February, 1902. From March until April 2d the symptoms increased. Examination by Dr. Putnam at that time revealed the following conditions:

Reflexes of flexors and extensors of forearms and of biceps and triceps very much exaggerated.

Reflexes of abdominal muscles and cremasteric reflex exaggerated; knee-jerks and ankle clonus and patellar clonus were very marked. Babinksi reflex present. There was a large bed-sore over the sacrum. There was no other trophic disturbance. There was no control over the bowels and bladder. Bowels were constipated and urine was voided involuntarily. There was total loss of sensation from the clavicle down, this being tested with an æsthesiometer and with heat and cold. Motion was entirely lost in the muscles of the left arm and leg. There was some power in all the muscles of the right arm and right leg. At that examination no contractures or muscular rigidity were observed.

The vision was good. Pupils contracted readily to light; left pupil was smaller than right.

A diagnosis of tumor of the third cervical segment of the cord was made, and operation was suggested as the only means for relief. The following day the case passed into other hands, under the promise of relief without surgical interference. The patient gradually grew worse, and on April 20th Dr. Krauss was called to make an examination, without knowledge of what had gone before or of the diagnosis of the previous examinations.

Careful examinations, both physical and electrical, covering several days, were made, and the diagnosis of spinal cord tumor of the third cervical segment was made, and an operation was urgently advised as the only procedure likely to afford relief. Dr. Roswell Park was asked to operate at this locality, and his report is here appended.

Report of the Operation. (By Roswell Park, M.D.) This was performed April 28, 1902. There was no difference of opinion as to the approximate location of the (supposititious) tumor; the lesion seemed to distinctly involve the third and fourth cervical segments of the cord.

Operation was made difficult by the shortness and stoutness of the neck. The incision extended superficially from the hair line down to the vertebra prominens. Chloroform was the anæsthetic used at first and mostly relied on. When the incision was begun he was breathing about eight times a minute. The position in which he was necessarily placed embarrassed his respiration still more. Before the separation of the muscles from the bone had begun he became cyanosed and ceased breathing. Artificial respiration was promptly resorted to, its necessity threatening to interfere with our antiseptic technique. Subsequent results showed, however, that our precautions were effective.

After thus restoring him the soft structures were rapidly separated on either side from the posterior vertebral surfaces; then with sharp cutting forceps the arches of the third, fourth, and fifth vertebræ were divided, the divided portions lifted and completely removed, and the spinal dura exposed for more than 4 cm. This membrane seemed a little dusky in hue and somewhat distended. With a sharp-pointed small knife I then punctured it at about the middle of the exposed area. Instantly there shot up to a height of at least a foot a tiny jet of cerebro-spinal fluid.

Within a few seconds after the intradural pressure was thus removed his respirations became more full and rapid, and within a few minutes had risen from eight to eighteen a minute.

The dura was then opened to the full length of its exposure. Projecting downward into this opening, partly concealed by the vertebral arch above, was a small tumor, reddish in color, and in appearance much like the choroid plexus, subdural, originating apparently in the pia-arachnoid, in length about 2 cm., its diameter a little longer than that of a common lead-pencil. It was not a difficult matter to detach it from the dura and from the sulcus, where it lay nestled, and then to pull it down from above, and so remove it, apparently, entirely. It was located rather to the right of the middle line, and its most distinct pressure was made upon the posterior columns of the right half of the cord.

The growth was not particularly vascular, and hemorrhage did not uncomfortably complicate the case at any time. As a matter of precaution, however, I applied adrenalin solution, 1 : 1000, on small tampons, and had the satisfaction of seeing the surface dry before closing the dura.

There being no apparent indication for any further intervention, I closed the dura with fine catgut and the balance of the wound with numerous buried sutures of catgut, and finally with silkworm-gut, without drainage. His condition at the conclusion at the operation was much more satisfactory than at its commencement. No plaster-of-Paris or other rigid splint for the head and trunk was used. The dressings were first changed on the third day, then not until the ninth. The wound healed throughout its entire extent by primary union. A microscopic study of the growth, made by Dr. Gaylord, in the State Cancer Laboratory, showed it to be a sarcoma of the round-celled type.

Subsequent History. The condition of the patient was extremely good after the operation, and he made an uninterrupted surgical recovery, which we must credit to the faultless technique of Dr. Park. During the ten weeks since the operation the following changes in his condition have been noted: Motion has returned to all the muscles of the right arm and leg. Sensation of the right side has not returned. Sensation has returned to *the left side*, but the muscles are still without voluntary power, so that at the time of the present writing the patient has the symptoms of Brown-Séquard paralysis—*motion on right side* and some sensation *on the left side*. The reflexes all over the body are still very much exaggerated. The bed-sore is healing under the influence of brewers' yeast. The urine is still passed involuntarily, but the patient is slowly improving. Each week shows increased muscular power and improved sensation. The paroxysms of pain have disappeared, the patient feels comfortable, is buoyant, and hopeful.

From a study of the literature of spinal cord tumors we believe our case to be unique for several reasons: 1. It is the only tumor of the spinal cord affecting the *upper cervical region* which has been so far recorded. 2. It is the only cervical cord tumor which has gone on to an uninterrupted course toward recovery. 3. It was definitely located and quickly removed without sacrifice of spinous processes and laminæ, and the short incision made a remarkably rapid closure. 4. The involvement of the phrenic nerve added an element of danger which was quickly removed during the progress of the operation. 5. From the surgeon's standpoint, it was located in the most inaccessible portion of the spinal cord, by virtue of the cervical curvature of the spinal column offering a concave field for operation instead of a convex.

STUDIES OF OVARIAN EMBRYOMATA, OR SO-CALLED OVARIAN DERMOID CYSTS.

By William Frederick Jelke, M.D.,
interne at the Lakeside Hospital, Cleveland, Ohio.

Everyone who has had the good fortune to study a series of ovarian cysts has found a certain small percentage of them to belong to the so-called dermoid variety. According to Olshausen, about 3½ per cent. of the ovarian cysts are of this kind. The so-called dermoid cysts of the ovary have given rise to so many conflicting views as regards their origin and structure that the literature is full of all kinds of polemics of which they are the subjects. Many of the older theories, themselves, seem to-day to be pathological curiosities. New theories as to their origin have, therefore, been received with a certain amount of reserve. The works of Pfannenstiel,[1] Kroemer,[2] and Wilms,[3] however, seem to have approached more nearly an ultimate solution of the problem than any that have appeared.

It is not the intention of this paper to introduce any new speculations concerning the origin of these tumors, but to describe as accurately as possible three so-called dermoid cysts of the ovary which have come to my hands for pathological diagnosis through the kindness of Dr. D. P. Allen, who removed them. Fortunately these three cysts represent quite distinct and separate features of this kind of new-growth in the ovary, and the study of them has yielded pathological findings similar to those described by Pfannenstiel, Kroemer, and Wilms.

Before beginning the description of these specimens it would seem proper, therefore, to mention briefly some of the conclusions reached by these men, which are exemplified by my pathological findings.

Wilms[3] showed that the so-called ovarian dermoids are to be held distinctively separate from the true dermoid cysts found in the head, neck, thorax, and other parts of the body. He also showed that the "embryome" or "zotte," which is the actively growing, or dynamic, portion of the cyst has representative tissues from each of the three primordial germinal layers, the ectoderm, the mesoderm, and the endoderm; that the order in which these tissues is produced is similar to the physiological process in the formation of the embryo. Accordingly, the skin, hair, teeth, etc.—ectodermal products principally—are the most conspicuous and most highly developed in the "embryome," while the visceral organs are seldom represented; for in the embryo the ectoderm and the cephalic end are differentiated and more highly organized long before the "anlage" of the splanchnic organs and the caudal end are differentiated. Further development to the complete embryo is soon turned aside by the hindrances of pressure and want of space, so that degenerative changes set in and pathological processes supervene which preclude any further development of the embryo as such. By stopping the process of development, thus, at any early stage, when the ectoderm is fairly well developed, the mesoderm less so, and the endoderm represented probably by merely a single layer of cells, it is evident that the last may be overlooked. Hence, it is easy to understand why, in some observations, the absence of representatives from the three primordial layers has been maintained, though a careful microscopic search will show them.

In the normal embryo there is an individual circulatory system very early in the life-history of the organism which is entirely separate from that of the mother, though it receives its soluble nutriment in the plasma through the placenta. In the so-called dermoid of the ovary, on the other hand, there is no placenta, nor is there even any decidual membrane formed in the uterus of the mother, which is one important point that serves to distinctly mark these structures from ovarian or abdominal pregnancies, in which cases an uterine decidua is always formed. The vascular system of the so-called ovarian dermoid is in direct continuity with that of the host without the intervention of a placenta, though, to be sure, new bloodvessels are formed as in all newly developing tissues, and in some cases even a more or less rudimentary bone-marrow is present which may subserve in a small way to the new-formation of blood corpuscles. Such a bone-marrow is found in Specimens 1 and 2.

Wilms then naturally comes to the conclusion that the so-called dermoid of the ovary is not of dermal origin, and is not a true dermoid, but he speaks of the new-growth as a "rudimentary ovarial parasite."

The Germans have referred for a long time to the actively growing portion of these cysts as the "embryome," in order to distinguish them from the true dermoids, which name they reserve for congenital cysts

containing skin, hair, etc., found elsewhere in the body and of different origin. A good translation of this term into English is "embryoma," and I shall use this in referring to the actively growing portion of the cyst in the following descriptions in contradistinction to the whole ovarian cyst, cyst wall, etc.

Pfannenstiel[1] and Kroemer[2] came to the conclusion that the embryoma is of ovulogenous derivation, and that it is not due to a maldevelopment of Pflüger's plugs or cell-nests; nor is it an example of parthenogenesis. They limit parthenogenesis to the physiological process by which a living individual is produced asexually for the purpose of maintaining a species. Pfannenstiel asserts that while the "embryoma" develops from the ovum, the cystic portion of the tumor is derived from the walls of the Graafian follicle.

Dr. J. G. Clark[4] reviews Kroemer's original work, and criticises it very favorably in *Progressive Medicine*, saying in conclusion: "It seems to me that Kroemer has furnished very strong arguments in favor of this theory, and if all his observations can be substantiated there can be no longer any doubt as to its correctness."

Kroemer comes to a full agreement with Wilms, who first offered substantial proof concerning the ovulogenous development of these tumors.

In describing the anatomy of these specimens it would be fruitless, and also beyond the limits of this paper, to go into minute details in respect to the shape assumed by each kind of tissue present, and all the details of its histology, since that would cover the greater part of a treatise on histology, for almost all of the principal tissues of the body are represented in these growths. Also, macroscopically the anatomy of each embryoma differs in greater or less degree from every other one. Therefore, only the more important findings which are characteristic of this kind of new-growth will be described. Also, the macroscopic and microscopic descriptions will not be completely separated, since the aid of the one will be called upon to elucidate or support the findings of the other. Where a conclusion may be drawn from the condition of a tissue found, it will be mentioned immediately, rather than separate these remarks from the picture in question.

Description of Three Cysts and Their Contents.

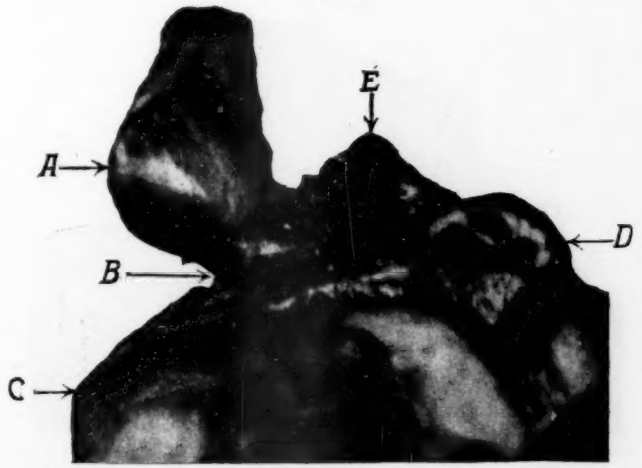
Specimen 1 (Fig. 1) was removed from Mrs. H. A., aged forty-eight years, nationality Russian. She had had eleven living children and two miscarriages. Family and personal histories unimportant, with the exception that sixteen years ago the patient was told she had a tumor in the pelvis about the size of a lemon. This increased gradually in size until some years later, when she began to feel the tumor herself

above the brim of the pelvis. The tumor caused no pain, nor did it interfere with repeated pregnancies.

The tumor was removed July 28, 1902, by Dr. Allen, on account of pressure and urinary disturbances it was causing.

Macroscopically the tumor is found to be a cyst of the right ovary, measuring 13 cm. in diameter and of 1½ litres content. The exterior of the cyst is of a dull yellowish white, in places shading into a bluish color. The surface is for the most part smooth, only here and there roughened by a few small tabs of fibrous adhesions. The right ovary and tube are adherent to the cyst, and also a portion of the fimbriated end of the left tube is adherent. Dark-blue bloodvessels can be seen radiating throughout the surface; they do not appear to be deeply

FIG. 1.



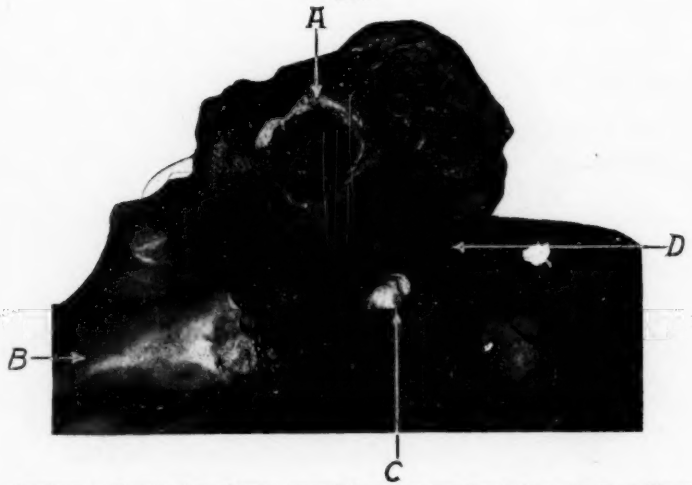
Specimen 1. Exterior of a portion of the cyst and adnexa. *A*. Cystic ovary. *B*. Bridge of tissue joining the cyst to a pole of ovary. *C*. External surface of cyst showing a few dark shadows of bloodvessels. *D*. Fallopian tube near uterine end. *E*. Fallopian tube near fimbria. (Natural size.)

situated in the cyst wall, but rather superficially. No inflammatory process, either past or present, can be made out in the ovary or tube. The former has a smooth exterior, except where attached by one pole to the large cyst; the latter is adherent only in part of its course, and its fimbriated end is free and patent; the lumen contains no pus. The wall of the cyst is very tough and leathery. In one place there is a small, thin area through which a hard body can be felt in the interior.

The lumen of the cyst is found to be unilocular, and to be filled with a thick, brown, pasty mass that has a faint aromatic odor. This mass

has a very greasy consistency when rubbed between the fingers. When exposed to the air at room temperature it rapidly solidifies and looks like beef fat or suet. Under the microscope it is composed of round balls of highly refractile, white-looking material. These balls or droplets dissolve readily in ether and warm alcohol, but separate out in cold alcohol or water. No crystals of cholesterin or other crystalline bodies are present. No leucocytes or other cells are seen, and no bacteria are found in the cover-slip preparations. Cultures tried on the usual media proved to be sterile. In the midst of this pultaceous mass is a ball of tangled, coarse, blonde hair. Almost all of the hair is found loose in the cavity, and is not attached to the inner surface of the cyst. The inside lining of the cyst does not resemble skin, nor does it

FIG. 2.



Specimen 1. Showing the embryoma everted through an opening in the cyst wall. *A.* Lip of ostium to the sac-like cavity in the embryoma. *B.* Cyst-wall, opened to show embryoma. *C.* Bicuspid tooth. *D.* Portion of the bone underlying soft parts. The black arrow indicates the direction of the transverse section surface shown in Fig. 4. (Natural size.)

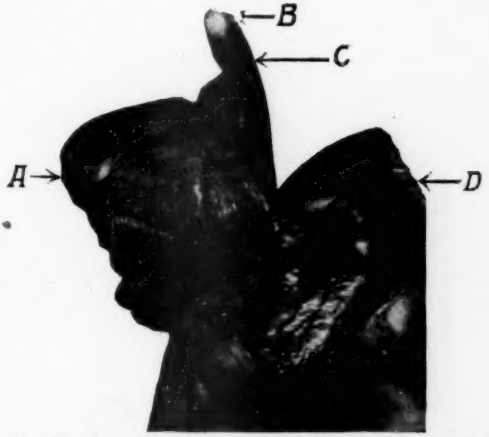
appear capable of bearing hair. Therefore, this large amount of hair must have been produced from the single point on the inside of the cyst wall from which the embryoma or "zotte" protrudes. Also, the fatty, sebaceous-like material derives its origin from the same source.

Projecting into the cyst lumen from its inner surface at a point 10½ cm. from the connection of the cyst wall externally with the ovary is a mass of bone and soft tissue. (Fig. 2.) This mass forms the "embryoma," and measures in this case 4½ x 3½ x 2 cm. A well-formed bicuspid tooth is seen projecting conspicuously from an exposed portion

of the bone. The bony portion of this structure is situated next to the cyst wall and underlies and supports the soft parts which cover the aspect turned toward the cyst lumen.

The shape of the bone is curved, the convex surface being turned toward the cyst wall. (Fig. 3.) This surface is completely flattened and smoothed. At the apex or the most prominent portion of the bone is situated a large bicuspid tooth. Now, at the first glance one is struck by the apparent resemblance of this portion of the bone to the lower maxilla in the adult. Due to its curved shape and the insertion of the tooth at the end, the total effect is that of an atrophied mandible in an old person who still possesses a single front incisor tooth, with the molar and bicuspid teeth lacking and an atrophied thin jawbone remaining.

FIG. 3.



Specimen 1. Another view of the embryoma showing the curved bone having the same curvature as the cyst wall. *A*. Embryoma, upper surface near the mouth of the cavity. *B*. Bicuspid tooth at apex of the bone. *C*. Convex surface of curved bone. *D*. Cyst wall. (About natural size.)

It is not the intention here to draw a close morphological comparison between this specimen and the senile lower jaw, but simply to show how far the imagination of the describers of many such specimens in the past has led them astray.

Some of the forces which produced the shape of this bone are made evident by noting its relation to the cyst wall. The curvature of the bone is that of a segment of a circle exactly coinciding with the inner surface of the cyst wall. The side of the bone next to the wall of the cyst is perfectly smooth and polished, and fits into a depression of the wall, which has likewise a smooth bottom. This depression in the wall has the exact outline of the bone, and serves as a matrix into which it is

set. There is no organic union between the bone and the cyst wall over this area, so that it is evident that the bone did not originate from the cyst wall, but is a lateral growth from the embryoma. It was through this thinnest portion of the wall that a solid body could be felt from the outside. When held up to the light one could almost see through this portion of the wall, it was so thin and translucent. In short, this thinnest area was produced by local atrophy, due to pressure on part of the bone. The surface of the bone, on the other hand, was made smooth and moulded so as to conform with the curvature of the cyst. The side of the bone toward the cyst lumen was free to develop, and hence had a more irregular outline, and at one point a tooth was produced. This tooth, however, is a bicuspid tooth, though it is in a position usually occupied by an incisor tooth, if this were, in reality, an attempt to form the lower maxilla. The side of the bone turned toward the cyst cavity was covered with a thin membrane, probably periosteum, while that facing the cyst wall was bare bone. Hence, the shape assumed by this bone was not due to a mimicry on the part of the embryoma to produce an organ similar to that found in the adult body, but it was moulded by external forces, to which it finally succumbed and resulted in a good example of pressure atrophy.

The soft parts are covered with a very coarse, hairy skin. The mouths of the large sebaceous glands are distinctly visible to the naked eye. The hair, however, has almost entirely fallen off. Directly above the point where the tooth appears in Fig. 2 is a globular, sac-like body, with a large round, smooth mouth. The wall of this structure is over 2 mm. thick, and is covered on the outside with fairly normal looking skin, which contains hair follicles, sebaceous and sweat glands. At the margin or lip of the ostium of this pouch a direct transition to smooth squamous epithelium void of hair or sebaceous glands takes place, and reminds one of the transition in the epithelium of the normal human lip. This same mucous epithelium lines the entire inner surface of this small cavity, which measures 2½ x 2 cm. A cross-section of it may be seen in Fig. 4.

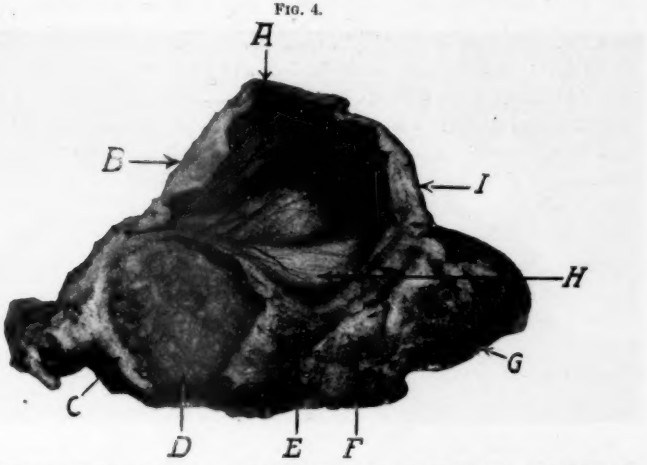
The wall of this cavity is constructed of fibrous and fatty tissues which surround the sebaceous glands that open toward the outer or skin surface, while the little cushion of fat and loosely held together connective tissue bulges toward the cavity on the inside.

The complete microscopic study of this specimen was greatly embarrassed by the profound hyaline degeneration that had taken place in the soft tissues, so that only good microscopic pictures could be obtained of the firmer tissues, bone, cartilage, and dentine. The reason for this hyaline transformation will be considered below.

A distinct zone of well-developed hyaline cartilage was found between the bone on the lower side and the soft structure above. Between the

cartilage and soft tissue a narrow strip of fibrous tissue could be seen. The bone presented near the centre a well-formed medullary cavity

FIG. 4.



Specimen 1. Cross-section of embryoma taken in a plane indicated by the black arrow in Fig. 2. *A*. Lip of ostium. *B*. Skin and hair-bearing surface, also showing a fat cushion bulging toward the interior of the cavity. *C*. Solid laminated bone. *D*. Bone-marrow. *E*. Site where corpora amylacea were found. *F*. Site of a large mass of cartilage. *G*. Cancellous bone. *H*. Internal surface of sac-like cavity lined with mucous epithelium. *I*. Skin surface of embryoma furnished with sebaceous glands and hair follicles. (Enlarged about twice natural size.)

filled with fat, red blood cells, and leucocytes of various kinds. This cavity was crossed by a few trabeculæ of cancellous bone.

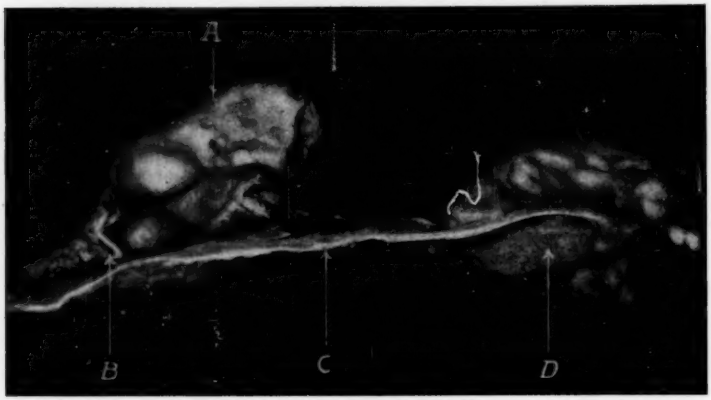
FIG. 5.

Specimen 1. X-ray photograph of embryoma showing five more teeth besides the one exposed bicuspid tooth at the top, which is the only one seen in the other photographs. (Natural size.)

At the point indicated in Fig. 4, *E*, a large group of corpora amylacea was found. As many as 175 were counted in one field

of the microscope with low-power objective. Some of the sections were stained in various ways so as to make sure of their composition.

FIG. 6.



Specimen 1. Showing the cyst wall intervening between and serving to join the ovary with the embryoma. *A.* Cystic ovary. *B.* Fimbriated end of Fallopian tube. *C.* Thin edge of cyst wall joining the embryoma to the ovary. The ovary extends on the external surface of the cyst wall, while the embryoma is situated on the inner surface and bulges toward the cyst lumen. *D.* Embryoma. (Reduced in size.)

FIG. 7.

Specimen 1. Corpora amylacea found at point indicated in Fig. 4, *E.* (Magnified about 80 times.)

They reacted typically to the iodine and sulphuric acid test, first made known by Virchow in 1854. Also, typical reactions were obtained with methyl violet and methyl green. That they also contained some calcareous material was evident from the avidity with which they absorbed hæmatoxylin. This fact suggested the possibility of their relationship to the psammoma bodies of the central nervous tissues, though in this case they were found in a degenerated glandular tissue. Morphologically, the usual hyaline-like layers were seen to be deposited around a bright, central, highly refractile nucleus, the whole body having a concentrically laminated structure.

These bodies were described first by Morgagni, in 1723, and have since, from time to time, given rise to much discussion concerning their nature and origin. Exhaustive studies on this subject may be found in the works of H. Stilling[5] and Ferdinand Siegert.[6] The general con-

FIG. 8.

Specimen 1. Section through cyst wall near the ovarian attachment. *A.* External surface of cyst wall, with remains of ovarian tissue. *B.* The line marking theca externa. *C.* Theca interna increased greatly in thickness by fibrous tissue, which is poor in bloodvessels. *D.* Layer of cells similar to corpus luteum cells.

sensus of opinion is that they are found in senile tissues more abundantly than elsewhere, as in the central nervous system, lungs, and prostates of old men, and that the tissues in which they are found have undergone atrophic degenerations.

The most interesting feature of this specimen is the fact that the embryoma is situated $10\frac{1}{2}$ cm. from the ovary which gave rise to it, as was mentioned above. The only connection of this body, which is considerably larger than the ovary, with the pole of the ovary which gave rise to it is by means of the thin cyst wall. This suggested the question: "From whence did the embryoma receive its blood supply and nutriment during the last sixteen years of its existence?" For we were assured by the patient that the cyst was the size of a lemon sixteen years ago. Thereupon, serial sections were cut out of the short pedicle between the ovary and the cyst, and also many sections were taken from the cyst wall lying between the ovary and the embryoma,

with the view of searching for the blood supply. It was found that there were very few bloodvessels present in the pedicle, and still less in the cyst wall, scarcely sufficient to supply the latter, much less the embryoma. The structure of the cyst wall was found to correspond with that of the ordinary corpus luteum cyst and to show two distinct fibrous layers of the theca externa and theca interna, the latter being very poor in bloodvessels, and in some places showing marked hyaline degeneration.

The interior of the cyst was lined with several layers of large cells irregularly packed together, containing large pale nuclei that resembled the corpus luteum cells lining a corpus luteum cyst. Hence, it became evident that the embryoma had developed in a Graafian follicle at one pole of the ovary. That the cyst wall had not taken part in the production of the embryoma, but it had remained a passive factor in the process, and that the lumen of the cyst had merely taken the place of a receptacle into which the loose hair, squamous cells, débris, and excretions of the sebaceous glands of the embryoma had discharged themselves. Thus, the constant increase in the contents of the cyst had gradually distended its walls and increased the size of the cyst; by increasing the size and periphery of the cyst the embryoma had been gradually carried away from the pole of the ovary from which it originated. The constant pressure from within had caused tension on the cyst wall, with a gradual occlusion of the bloodvessels supplying the embryoma.

This cutting off of the blood supply would easily explain the general hyaline degeneration that had taken place in the embryoma.

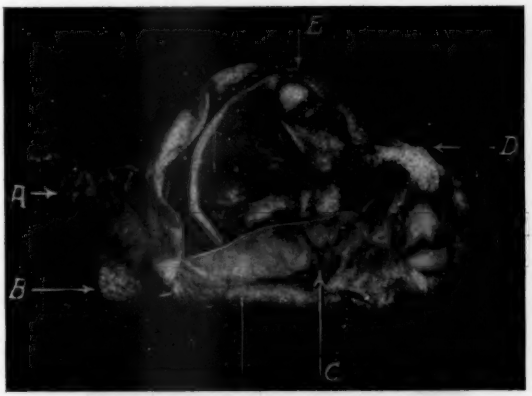
The X-ray photograph shows five more teeth besides the one large exposed bicuspid tooth. These teeth were inserted in the cancellous bone underlying the soft tissues, and had not yet cut through to the surface, and their presence was not discovered until the shadow was obtained on the X-ray plate. Sections were studied from the ovary which was removed with the cyst, and it was found to contain several small follicular cysts; two of them measuring over 1 cm. in diameter. There are no normal follicles to be seen in the cortical portion, and the stroma shows a general senile atrophy.

Specimen 2 was removed from Mrs. B. S., aged twenty-two years; nationality Russian. Family and personal histories unimportant until thirteen months ago, when she was in confinement. Since then she has complained of pain in the lower portion of the pelvis, which has greatly increased during the last six weeks. She was operated on May 23, 1902, by Dr. D. P. Allen, who removed a tubo-ovarian mass from the left side, which was greatly inflamed. This mass on fresh section was composed of clotted blood and a soft spongy tissue, which, on further microscopic study, proved to be an early tubal pregnancy. From the right side was removed the specimen here to be described.

The Fallopian tube on the right side is found to be normal. The ovary on this side is normal in size, measuring 4 x 4 x 3 cm., but is soft and studded with small cysts about the size of a pea. These were found later to be the maturing Graafian follicles. The surface of the ovary is white and glistening, and shows no signs of inflammatory reaction; there are no adhesions on this side. Upon section of the ovary it is found to be filled with a yellow, thick, semifluid material, which is quite greasy. Cultures grown in the usual media remained sterile.

After carefully removing this semisolid mass, in which were found a few loose hairs, a small portion of bone was exposed, in which was inserted a bicuspid tooth. Near one end of this plate of bone a soft,

FIG. 9.

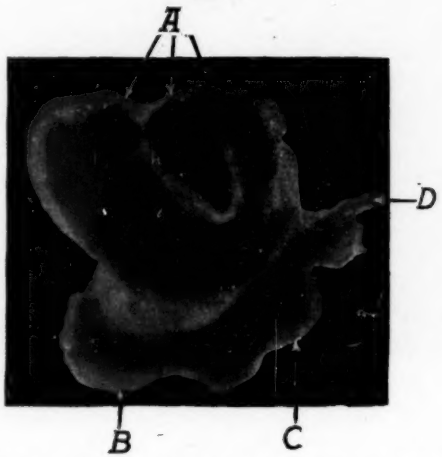


Specimen 2. Shows the ovary opened by a longitudinal incision. *A*. Fimbriated end of Fallopian tube. *B*. Fallopian tube. *C*. External surface of ovary and wall of cyst, showing small cystic follicles on uneven surface. *D*. Embryoma, with soft tissue and tuft of hair. *E*. Bony portion of embryo and single bicuspid tooth.

irregular spongy body was found covered with skin, from which protruded a small tuft of hair. The bony portion seemed to arise from one side of the cyst only, and occupied about one-third of the inner surface of the cyst; the latter was drawn over the remainder of the embryoma as a sac-like covering. In other words, this is the same condition as was found in Specimen 1, only in this case the cyst is much smaller in proportion to the embryoma. Here the embryoma fills almost the entire cyst lumen, and the greater portion of the embryoma, macroscopically, is seen to be composed of bone, while the skin and hair-bearing surface is reduced to a small area of about 1 x 1½ cm. In the former case, Specimen 1, the skin and hair-bearing surface was considerable, covering the greater portion of the embryoma, and, conse-

quently, the cast-off hair and excretions from the skin formed the largest and most conspicuous portion of the cystic contents. Here, then, is good evidence that the cyst lumen serves chiefly as a receptacle for the excretions from the dermal surface of the embryoma, and that the size and distention of the cyst are in direct ratio to the amount of waste products shed from the embryoma. The shape of the bone was fairly regular and disk-shaped, with two small undulating prominences, which, on comparing with the X-ray shadow, were seen to be the site of two teeth not yet cut through the surface. This was substantiated later by transverse microtome sections. This bony portion of the embryoma was covered with a thin, firm, smooth tissue that had a moist, sticky surface entirely void of hair and not resembling normal skin, but looked more like mucous membrane.

FIG. 10.



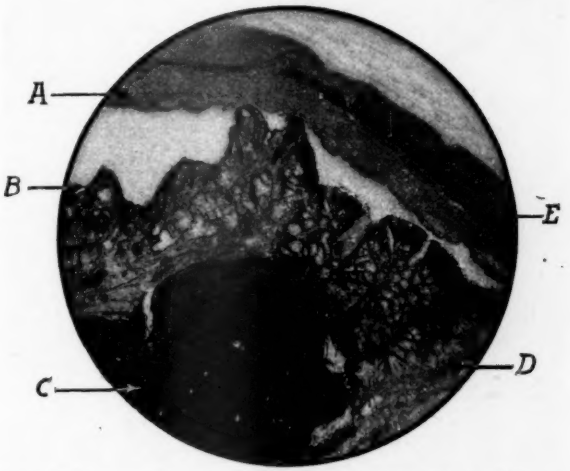
Specimen 2. X-ray photograph showing two more teeth in addition to the single bicuspid tooth in Fig. 9. *A*. The three teeth. *B* and *C*. Fallopian tube. *D*. Fimbriated end of Fallopian tube.

After this superficial investigation, the longitudinal incision through the cyst wall was tightly sutured, so as to restore as nearly as possible the relation of the embryoma to the cyst. The whole mass was then decalcified, and sections were cut.

Microtome sections were cut transversely to the long axis of the ovary through the cyst wall, soft parts, bone, and teeth. The cyst wall is seen to contain ovarian stroma in all portions, so that the embryoma, which is centrally located in the ovary and arises from the thickest part of the cyst wall, must have arisen in a Graafian follicle near the medullary portion of the ovary, and not in the cortical portion.

The soft parts are covered with a true skin at the end of the embryoma, from which the tuft of hair may be seen growing. This skin is remarkable in the great amount of comedone formation present. That is, the ducts of the sebaceous glands have become stopped, and minute retention cysts have formed, which have subsequently broken through to the surface, causing the skin to have a very rough, uneven, honey-combed appearance. The epidermis is normal, having a well-defined corneous layer, and shows the transition from squamous to polyhedral cells in the deeper layers. The corium is well developed and contains fibrous and fatty tissue, which is penetrated by the hair shafts springing from

FIG. 11.



Specimen 2. Microscopic section through a portion of the cyst wall and embryoma. *A.* Cyst wall containing ovarian tissue. *B.* Epidermis of embryoma thrown into an irregular, broken surface by the comedone formation in the sebaceous glands. *C.* Firm lamellated bone showing Haversian canals. *D.* Corium of skin containing large masses of sebaceous glands. *E.* Cyst wall containing a long flattened corpus albicans in the ovarian tissue. (Magnified about 40 times.)

normal hair papillæ. The size and number of the sebaceous glands are far greater than normal, and hence, the condition may be looked on as an hypertrophy and proliferation.

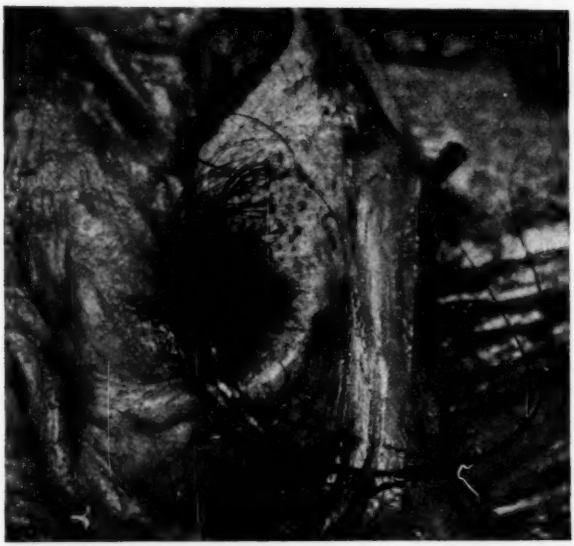
Around the bases of these glands is seen the fibrous tissue of the corium held together in loose bundles; in other places fat cells are more predominant.

In the corium are seen masses of tubular glands lined with a single layer of low cuboidal epithelium, with large round deeply staining basal nuclei. These cells rest on a firm homogeneous highly refractile narrow band of tissue that may be considered the membrana propria, which

separates the gland tubules from the connective tissue of the stroma and from each other. These glands, without doubt, bear a strong resemblance to sweat glands; but, due to the great number of sebaceous glands above them, it is difficult to find ducts long enough to penetrate in one continuous line to the surface of the epidermis in one section, though cross and oblique sections of such ducts are frequently seen.

The soft parts at the other end of the specimen show a rather complex set of foldings and reduplications. Here the epidermis is quite

FIG. 12.

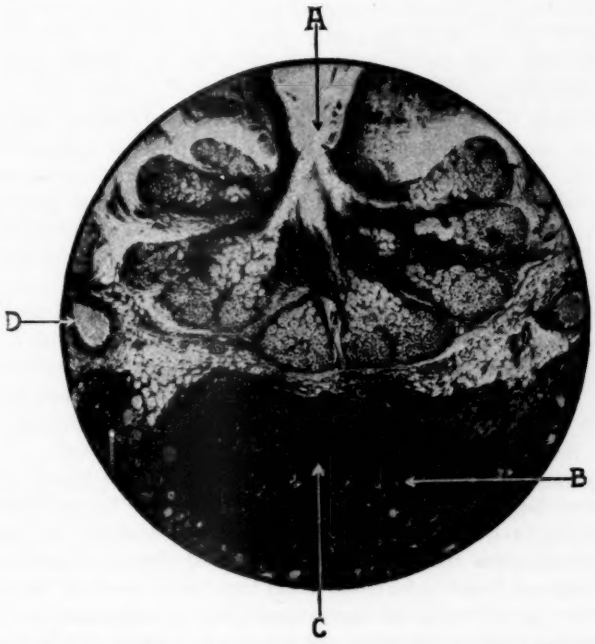


Specimen 3. Interior surface of cyst wall, showing the flattened embryoma. The tuft of hair is seen springing from the skin surface, which is dotted over with large mouths of sebaceous glands. (A trifle enlarged.)

thin, though of the squamous variety; it contains no papillæ, and is only four or six cells deep in some places. No glands of any description underlie this epithelium. There is a marked change in the surface, which rises up to form regular papillæ or villi, covered with low columnar epithelium, with round vesicular nuclei placed at the base of the cell. Where cross-sections of these villi are met they are seen to be uniformly round or oval in contour; and the epithelial cells rest on a fine basement membrane. The body or core of the villus consists of fibrous connective tissue regularly placed around small vessels. A few leucocytes and red blood corpuscles are seen in the meshes of the con-

nective tissue. These structures then resemble closely the villi of the small intestine. On following this undulating surface into some of the other folds, a transition from squamous epithelium to high columnar ciliated epithelium is seen. These columnar cells have large, oval basal nuclei. Between them are placed many interstitial cells, and the whole mucosa is bounded by a distinct limiting membrane. This tissue is seen to contain many small round deeply stained leucocytes, and in

FIG. 13.



Specimen 3. Microscopic photograph showing representatives from the three primitive layers. *A.* Epidermis with the mouth of an immense sebaceous gland. *B.* Rudimentary thyroid gland containing colloid material in the acini. *C.* Large mass of lymphoid tissue. D. Bloodvessels in corium surrounded by fibrous and fatty tissue.

some fields of the microscope they are found massed together into structures resembling solitary follicles.

The more highly differentiated glandular structures found in the normal intestinal wall, like the glands of Brunner and the follicles of Lieberkühn, are absent.

The bone in this specimen is macroscopically irregular and of a nondescript form, but microscopically it contains all the structures of

normal bone. A large portion of it has a cancellous structure, and the spaces are filled with red and yellow marrow. The teeth have all the structures found in normal teeth. The dentine is laid down in perfectly parallel dentinal tubules, and the pulp cavity is seen to contain normal bloodvessels and fibrous tissue.

The sections through the remainder of the ovary lying outside of the cyst wall show numerous Graafian follicles in various stages of maturity, and some of the follicles are so large as to become small cysts. These large follicles are situated in the cortex of the organ, but there is still considerable dense ovarian stroma separating them from the surface. It is rare to see so many apparently mature follicles and others rapidly approaching maturity in a single section as the sections from this specimen show.

Specimen 3 was removed from Miss I. W., aged twenty-five years; teacher; nationality American. Family and personal histories unimportant. During the last two years she has had some uterine trouble and has complained of increased frequency in menstrual periods, for which she received local treatment. On September 4, 1902, Dr. D. P. Allen removed the specimen, now to be described, from the left ovary.

This consists of a cyst measuring 12 x 9 x 7½ cm., or about the size of a large orange, weighs 460 grammes, and is ovoid in shape, with a fairly regular outline. The exterior has a glistening, pale, yellowish-white color. No adhesions are present. The tube is firmly stretched over the cyst in the middle of its course, but both ends are free and patent. In short, there are no evidences of inflammation past or present.

The exterior of the cyst is of a light-yellow color, in places shading to a dark blue or purple. Immediately after removal the cyst appeared to contain fluid, and fluctuation of its contents was noted; by the time the operation was over, however, it had cooled down to room temperature, and was found to be much firmer than when removed; fluctuation could not be obtained, but the contents could be kneaded like putty. It was then evident, before the cyst was opened, that it belonged to the variety that we are now considering.

On opening the cyst it was found to be filled with a light-yellow, greasy material which resembled butter. This was thoroughly mixed with a tangled mass of dark-brown hair. Cultures grown on the usual media remained sterile.

The oleaginous portion of the cystic contents was easily soluble in ether and warm alcohol, but not in cold alcohol or water. When examined under the microscope it was seen to be made up of small, highly refractile balls or droplets. A portion of it was treated with a dilute solution of warm potassium hydroxide, and it was saponified. No cholesterin or other crystals were found, nor were there any leu-

cocytes to be seen, but merely the desquamated epidermal cells and débris.

In this case the cyst was bilocular, that is, there were two large loculi; one, however, about twice the size of the other, contained the hair, and in this one the embryoma was found. The smaller cyst contained a thick, viscous fluid, partly mixed with the oily substance derived from the other cyst, for a small perforation was found in the septum between them.

The embryoma was found quite flattened against one side of the cyst, and appeared directly continuous with the ovary, which was flattened and stretched on the outside of the cyst. The shape of the embryoma was more irregular in this case than in either of the others, but, in general, it assumed that of a bar or bridge of tissue stretching across a segment of the cyst and having irregular expansions on the cyst wall at either end.

FIG. 14.

Specimen 3. X-ray photograph showing the small almond-shaped piece of bone with one tooth lying in the centre of the embryoma, which shows in lighter shadow.

The side of the embryoma turned toward the cyst lumen had a large superficial expansion, and was covered with hair and the mouths of large sebaceous glands. The lower or under side of the tumor was covered with a smooth, almost velvety epithelium, possessing no hair or visible gland orifices.

This embryoma is the smallest of the three, measuring 5 cm. long by 2.2 cm. wide, but has relatively the largest skin and hair-producing surface. The size of the cyst, though not actually so large as Specimen No. 1, was relatively to the embryoma very much greater. Here, then, was a large cyst with a relatively large skin and hair surface on the embryoma. In other words, this substantiated the fact above noted, that the cyst serves simply as a receptacle for the excretions of the embryoma, and where a large cyst is present a correspondingly large surface for the production of the cystic contents must naturally be expected. In Specimen No. 2 the skin and hair-producing surface was

seen to be quite small; in that case the cyst did not go beyond the limits of a normal sized ovary. Only one hard, firm nodule, about the size of an almond, could be felt in the body of the embryoma. This was shown by the X-ray shadow to be composed of a small piece of bone and one tooth. (Fig. 14). No teeth were visible on the surface of the embryoma. The line of demarcation between the skin covering the embryoma and the interior surface of the cyst wall was very distinct.

In the macroscopic description it was noted that the embryoma was attached at either end to the cyst wall, but was free in the cyst lumen near its central portion. One of these ends was seen to arise opposite the point where the ovary was attached on the other side of the cyst wall; for the sake of convenience in the description this will be designated the proximal end of the embryoma, being nearest the ovary, while the other end will be referred to as the distal end. Microtome sections were begun at the proximal end and cut transversely to the long axis of the embryoma.

The first set of sections were carried through the ovary, cyst wall, and proximal end of the embryoma. The layer of ovarian tissue is seen to be very much flattened and thinned with the cells of the stroma densely packed together.

Next to this is the cyst wall, composed of dense strands of fibrous tissue laid in parallel bundles. The cyst wall in this case is the one most richly furnished with bloodvessels of the three specimens. A definite arrangement of the layers into a theca interna and theca externa can be made out as in the other two cysts.

The proximal end of the dermoid is composed chiefly of loosely packed connective tissue, which is well supplied with large bloodvessels. Some of the intervascular connective tissue is seen to be undergoing an apparent myxomatous change. In these areas the cells are seen to be greatly swollen, the cytoplasm being pulled out into long, thin processes, which take a very faint eosin stain. Some of the cells appear purple on account of the indifferent way in which they take both the hæmatoxylin and eosin. The nuclei still retain their staining properties, though they are large, pale, and vesicular.

In some places where the change is most extensive only the nuclei can be seen, the cytoplasm and intercellular substance no longer being differentiated by the stains. Such areas look very much like soft, medullary, sarcomatous tissue. The altered tissue does not appear malignant, however, and such changes in ovarian tissue and ovarian tumors are not uncommon. There are numerous small, round, lymphoid cells throughout this portion of the preparation, and here and there they may be seen massed into large groups that appear like lymph nodes. The upper and lower surfaces of the embryoma near the proximal end are covered with squamous epithelium; that on the upper surface is

thicker than that on the lower, though no hair follicles or glandular structures are to be seen in this portion of the specimen.

The next block of sections was taken from the middle portion of the embryoma, and involved the soft parts and the bone discovered by the X-ray shadow. The upper surface or side of the embryoma turned toward the cyst lumen in these sections is that portion which is seen to be so richly supplied with hair. Here the epidermis is of normal thickness, but the corium is very much increased in depth on account of the large number of hair shafts and the great increase of sebaceous glands that dip down into it. A definite pigment layer is easily made out in the epidermis in this case. Below the sebaceous glands a narrow band of non-striated muscle is seen weaving its way in a wavy outline across the specimen near the fundi of the sebaceous glands. Bundles of nerve tissues are also easily made out. These bundles appear like the trunks of normal peripheral nerves, composed of axis-cylinder and myelin sheath. These bundles can be traced into the next set of sections taken from the distal end of the embryoma, in which ganglion cells are found.

Islands of cartilage of various sizes, with perfectly normal cells, are present. Some of these islands are long and narrow, and it is evident that an attempt has been made to form a chain of strips or islands of cartilage, but a complete ring has not been formed, such as occurs in a normal trachea. As the lower side of the section is approached (corresponding to the lower side of the embryoma), the connective tissue is less dense, and here and there is replaced by islands of fat. Large masses of lymphoid cells are also met. Finally the lower border of the section is seen to be covered with a single layer of ciliated columnar epithelium. The small section of bone in this specimen is quite dense, and no cancellous tissue is present. The arrangement of the lamellæ and Haversian canals is normal.

The third set of sections, involving the cyst wall and the distal end of the embryoma, shows the same great variety of tissues as the preceding sections. In addition, a rudimentary, mucous, salivary gland, showing all the details of the normal structure, including acini and tubules, is present. These tubules are quite distinct, and the acini are separated by a considerable amount of fibrous tissue; the definite racemose character of the glands is well marked.

Tissue resembling normal thyroid gland, with well-marked spaces filled with colloid material, is present. One of the most interesting histological details of the sections from this part of the embryoma is the well-developed ganglion containing large nerve cells, such as are seen in the dorsal root ganglia of the spinal sensory nerves.

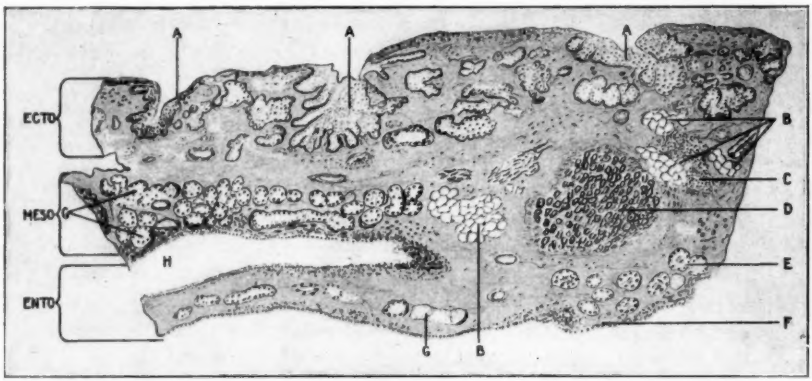
Space would not permit, here, to go into all of the histological details of the representatives of the various glands, tissues, and structures occurring in the upper portions of the respiratory and alimentary tracts

found in this specimen. Such would be merely a repetition of well-known histological pictures.

Taking the general relation of these structures to one another into consideration, however, it is interesting to see that they had a fairly definite order, beginning with the ectodermal derivatives on the superior surface (the skin, hair, and sebaceous glands), followed by the mesodermal structures (connective tissues, bone, fibrous tissue, cartilage, etc.) near the centre of the embryoma, and finally furnished with the derivatives of the endoderm (the ciliated columnar epithelium, thyroid gland, and a structure similar to the intestinal canal) near the lower surface of the embryoma. (Fig. 15.)

The most extensively developed layer is the ectodermal, the least differentiated the endodermal.

FIG. 15.



Specimen 3. This is a photograph of a drawing made with a camera lucida of a section showing the representative tissues derived from three primordial layers. The outlines are perfectly preserved, though the nuclei were put in free-hand and show up too large in proportion to the magnification. *A.* Large sebaceous glands. *B.* Fat. *C.* Lymphoid tissue. *D.* Cartilage. *E.* Thyroid tissue. *F.* Ciliated columnar epithelium. *G.* Salivary gland tissue. *H.* Cavity lined with ciliated columnar epithelium. *Ecto*, *Meso*, and *Ento* represent in a general way the three zones of the embryoma in which representatives from the three primordial germinal layers may be found. (Magnified about 12 times.)

The cells representing these tissues are in every case as perfect of their kind as those found in normal adult organs; but, on the other hand, the organs themselves have in no case reached a normal and full completion. In other words, the picture produced is that of normal adult cells placed in the positions of embryoidal beginnings of organs. The necessary foldings and mechanical action in the migration of the various cells has not taken place. To use a military simile, one might aptly describe the position of these adult cells as one in which no mobilization had

occurred, or in which they had not been mustered into their proper ranks.

The bizarre form assumed by the tissues of this and other specimens would then be explained as in Specimen No. 1, namely, that extraneous forces had so hemmed the development along normal lines as to sooner or later arrest the growth. Also, the fact must not be forgotten that here a large portion of the embryoma is held stationary against the cyst wall, so that the normal foldings and invaginations of the various tissues cannot take place as in the normal embryo, which is practically swung free in space in the amniotic fluid.

SUMMARY. 1. It has been shown in these specimens just described that, though each has an anatomy peculiar to itself, still there is much in common among them, and also that they are similar to the cases recorde[1] by Pfannenstiel, Kroemer, Wilms, and others.

2. Structures derived from the three embryonal primordial layers were found in each of them, with the exception of the first, and here the microscopic search for the endoderm was prevented by the great degeneration of the tissues, so that only the coarser structures could be made out.

3. The extent of the development along different lines varied greatly in each case, though all of them were turned to pathological growth comparatively early when compared with the normal embryo.

4. The structure of the cyst wall was seen to be similar to other cysts derived from Graafian follicles.

5. The size of the cyst was independent of the size of the embryoma within certain limits, but the size of the cyst seemed to vary in direct proportion to the amount of waste matter excreted by the embryoma.

6. The remains of the ovary from which these specimens developed, as well as the organ on the opposite side, were found to be either cystic or to have an abnormally large number of follicles approaching maturity.

7. In none of the specimens were any fœtal inclusions, fœtal remains, or congenital malformations found, and that the rest of the genitalia of the hosts was normal with the exception of the cystitis in Case I., and the tubal pregnancy in Case II. So that the congenital formation of these tumors appears extremely doubtful.

It seems necessary to mention, however, for sake of completeness, that such congenital origin for these new-growths has been maintained by Bandler[7] since the works of Pfannenstiel, Kroemer, Wilms, Arnsperger,[8] and others of recent date have appeared. A review of Bandler's work is found in *Progressive Medicine*[9] of June, 1902, so that it will be unnecessary to go into detail concerning it here, but simply to mention that he tries to prove the origin of these cysts to come from the remains of the Wolffian duct and misplaced ectodermal cells.

The cause of this apparently spontaneous segmentation on the part of the ovum is an unsolved problem, as is the cause of the proliferation of certain other cells to tumor formation; but the process is considered to be an analogous one by some of the recent investigators on the subject.

Arnsperger[8] says: "The fact that the maximum for the frequency of dermoids coincides with the height of the sexual life is important. This fact then speaks more for the derivation of ovarian dermoids from the ripe ova. I believe that if all dermoids (of the ovary) were congenital, more would be found at the autopsies of children."

It is significant that in many cases of so-called dermoids of the ovary there have been various other cysts and new-growths in combination with them.

Klein[10] states that 14 per cent. of the ovarian embryomata are combined with other types of cysts of the ovary. He reports one case in which a threefold combination was present in the same ovary, namely, an embryoma, a colloid cystoma, and a malignant tumor. Niemer[11] also reports several cases of combination of dermoids with other cysts of the ovary.

A case of Simmerling[12] has been reported, in which a proliferating glandular ovarial cystoma was found complicated with a small carcinomatous dermoid cyst.

Pfannenstiel[13] goes further and says: "The same impulse which causes the production of malignant tumor formation induces the formation of the dermoid cyst. From the epithelium of the Graafian follicle develops a simple cystoma or a pseudomucin cyst." He says, in another place, that ovarian dermoids are most frequently found combined with pseudomucin cysts.

Wilms[14] says that when we bring the two tumor groups in relation to each other, the embryomata of the testis and the embryomata of the ovary, with tumors in general, then we must consider them the most complex of all tumors. In his last contribution to the subject Wilms* defines the so-called dermoid cyst of the ovary as follows: "The embryoma of the ovary is a tumor composed of a threefold germinal anlage ultimately derived from an ovum, which, during its development in a small cyst, is early arrested, and only succeeds to the rudiment of an embryo."

TECHNIQUE. When the macroscopic description of the first specimen was begun it became evident that it would be very much simpler to record the gross appearances of these bizarre tumors by means of

* M. Wilms' definition of the embryo: "Das Embryome des Eierstockes ist eine aus einer dreiblättrigen Keimanlage in letzter Instanz, also aus einer Eizelle hervorgegangene Geschwulstbildung, welche durch die Entwickelung in einer kleinen Cyste in ihrem Wachsthum frühzeitig gehemmt, nur zu einem Rudiment eines Embryo auswächst."

sketches and photographs than by long verbose protocols; for in each instance there was an individual anatomy to deal with and no standard for comparison. Therefore, liberal use of the camera supplemented by explanatory sketches was employed throughout the study of them. The accompanying illustrations are some of the many views taken.

Since bone and teeth composed such a large part of the tumors, X-ray photographs of the specimens were taken in order to obtain the quantity and relation of the bone to the soft parts, and in each of them teeth hidden either in the bone or soft tissues were discovered. This proved of great value when it came to dividing up the material for microscopic study, and was the means of saving many a microtome knife; for, by comparing the specimens with the X-ray plate, one could tell exactly the points where to expect buried teeth and dense bone. Such pieces were left for a longer period in the decalcifying fluid.

On account of the close relationship of the bone, which was present in large masses, to the soft parts, it was necessary to decalcify the former without injury to the latter.

Most of the methods of decalcifying teeth and bone in large pieces, found in the various books on laboratory technique, do not give perfectly gratifying results in all respects. Either the bone is sufficiently decalcified and the staining characteristics of the soft tissues sacrificed, or the bone remains too hard to cut, and the soft parts are preserved. The weak solutions of acids take entirely too much time in the routine preparation of large pieces of bone for microscopic study, and daily changing of the decalcifying fluid is necessary over a period of several months. The use of phloroglucin as a protective with very strong acid is expensive, on account of the comparatively high price of phloroglucin as a laboratory reagent, and a long period of washing is necessary to remove the excess of acid, so that this method is not altogether satisfactory for large pieces of bone.

The ideal method for decalcifying bone and teeth, then, is one in which the insoluble organic salts may be removed in a short period of time, leaving the soft organic structures in their natural forms without marring the staining properties of the cells.

In preparing the above specimens for microscopic study the following steps were taken:

1. The specimen was hardened *en masse* by placing it in Orth's fluid for three to four days.

(Orth's fluid = Müller's fluid plus 4 per cent. formaldehyde.)

2. Washed in running water for twenty-four hours to remove the excess of this fluid, since a dark brown precipitate occurs in tissues left too long in Orth's fluid.

3. Removed from the running water and placed directly in the following decalcifying fluid:

Pure nitric acid from 75 c.c. to 100 c.c. (according to the density and size of bone, and the speed desired in decalcification); alcohol (95 per cent.), 750 c.c.; distilled water, 250 c.c.; sodium chloride, 7½ grammes.

This is a slight modification of von Ebner's decalcifying fluid.

The fluid was made up in this manner in quantities. The specimen was placed in a glass jar fitted with a tight screw top, to prevent loss of the alcohol, containing from 150 c.c. to 200 c.c. of this fluid at a time, according to the size of the specimen. The fluid was changed on an average of every four to five days until complete decalcification was obtained. This was ascertained by thrusting a fine needle into the portions of the specimen where the X-ray shadows indicated the firmest bone and teeth.

4. The specimen was transferred from the decalcifying fluid to the alkaline neutralizing fluid, composed of: aqua ammoniæ fortior, 10 c.c.; alcohol absolute, 90 c.c. It remained in this fluid twenty-four hours.

5. Alcohol and ether in equal parts.

6. Embedding in celloidin as usual, etc.

The results obtained by this method were very gratifying, not only in the sections obtained of the above specimens, but also of bone from other sources, such as osteomyelitis, epiphysitis, and teeth. The advantages of this method are in a general shortening of several of the steps usually taken in decalcifying, the uniformity in which the decalcification takes place, and the perfectly retained staining properties of the soft tissues.

It will be noticed that after hardening in Orth's fluid and washing in water the specimen is transferred directly to the decalcifying fluid. By the other methods usually employed the partial softening and swelling of the tissues incident to washing after Orth's fluid has to be overcome by a second hardening in alcohol before the decalcification process is begun. This, of course, takes time.

By using a decalcifying fluid that contains a high percentage of alcohol this is not necessary, for the alcohol in the decalcifying fluid serves as a hardening reagent to the soft parts, while the solid inorganic salts are attacked by the acid. Also, the presence of the NaCl in a quantity sufficient to bring the density of the fluid to about that of normal salt solution is a great protection to the soft parts, since it prevents the setting in of strong diffusion currents through the tissues, and the imbibition of water which would tend to swell and distort the cells.

Instead of removing the excess of acid by a prolonged washing of the specimen in running water, as is usually the custom, it is transferred immediately to a stronger alcoholic solution made alkaline by ammonia.

This is not only a saving of time in this step of the process, but also makes it unnecessary to submit the tissue to the dangerous process of too long washing and swelling of the decalcified tissues by imbibition. Ordinarily after such washing the specimens have to be rehardened by carrying them through graded alcohols before embedding. I believe that tissues are almost as frequently spoiled in decalcification processes by transferring them from alcoholic to aqueous solutions, and in and out of hardening and decalcifying fluids of different osmotic equivalents, as they are by too long contact with acids, or by using too strong acid solutions. The above decalcifying fluid varies from von Ebner's fluid in the use of HNO_3 instead of HCl, and in different proportions of the other ingredients.

By using an ammoniacal strong alcoholic solution to neutralize the excess of acid much time is saved, and the specimen is kept continually in a hardening fluid from the time it leaves its initial washing following Orth's fluid. The use of ammonia is preferred also to that of other alkaline reagents, such as $CaCO_3$, $NaHCO_3$, etc., since it may be used in almost any desired concentration and excess without injuring the tissues and without introducing an alkaline reagent that might reprecipitate some of the mineral salts which have been dissociated by the acid, but which may still remain in the tissues.

The extreme solubility of most ammoniacal salts precludes this. Also, a mineral alkaline body, if left in the tissues in excess, would interfere with the subsequent staining, since tissues should be neutral in reaction, in order to obtain satisfactory histological stains. The excess of ammonia, however, completely evaporates by the time the specimen has been carried through the alcohol and ether and embedding process and has been sectioned ready for staining. In several cases after the sections had been cut they were placed in a bottle with a small quantity of water, and vigorously shaken, so that any excess of free ammonia would be washed from them. This wash-water was then tested with litmus paper, and was found to be neutral.

Another characteristic of this process is that when this specimen is transferred from the decalcifying fluid, containing the nitric acid, to the neutralizing fluid, containing the ammonia, a bright-yellow or orange color is given to the specimen. This color is due to the well-known xanthoproteic reaction, which takes place in proteid bodies when treated with these reagents. This color, however, does not in any way detract from the staining of the cytoplasm of the cells with eosin. In fact, in many of the sections advantage was taken of this color reaction as a contrast to the nuclear stain, and then only hæmatoxylin was used. Whether this yellow color will persist or not, as eosin will for a long time, is doubtful.

In describing Specimen 1, it was stated that the whole embryoma had undergone such profound hyaline degeneration as to prevent a satisfactory microscopic study of it. At first it was feared that this hyaline degeneration might be an artefact caused by the strong decalcifying fluid, so a portion of the soft tissues from the other half of the embryoma and cyst wall that had not yet been decalcified was cut from the bone and carried through in the ordinary manner for soft tissues without coming in contact with the decalcifying fluid as a control test. When this was cut and stained it was found to behave toward the staining reagents in the same manner as the portion that had been decalcified. This proved that the decalcifying fluids had nothing to do with the poor staining properties of Specimen 1, but that a true hyaline degeneration had taken place.

Specimens of bone and teeth from various sources, combined with more or less soft tissues, have been decalcified by this method in pieces of 1½ cm. square in less than three weeks, which would have taken at least six to eight weeks by the ordinary methods, and they have retained their staining properties perfectly.

Bibliography.

1. J. Pfannenstiel. Die Erkrankungen des Eierstocks und des Nebeneierstocks, Veit's Handbuch d. Gynäk., 1897. Verhandlung d. deutschen Gesellschaft. f. Gynäk., Leipzig, 1897.

2. P. Kroemer. Ueber die Histogenese der Dermoidkystome und Teratome des Eierstocks, Archiv f. Gynäk., Bd. 57, Berlin, 1899.

3. M. Wilms. Ueber die Dermoidcysten und Teratome, mit besonderer Berücksichtigung der Dermoide der Ovarien. Festschrift von Zenker, Deutsches Archiv f. Klinische Medicin., Bd. lv., 1895. (This contains a very full bibliography.) Chapter in A. Martin's text-book, Die Krankheiten der Eierstöcke und Nebeneierstöcke, Leipzig, 1899.

4. J. G. Clark. Review of Kroemer's article, Progressive Medicine, June, 1899, p. 159, Histogenesis of Dermoid Cysts and Teratomata of the Ovary.

5. H. Stilling. Entstehung von Concrementen der Prostata, Virchow's Archiv, Bd. xcviii, 1884.

6. Ferdinand Siegert. Untersuchungen ueber d. Corpora amylacea, Virchow's Archiv, Bd. cxxix., 1892.

7. S. W. Bandler. Dermoid and Other Cysts of the Ovary, American Journal of Obstetrics, June, 1901, vol. xliii.

8. H. Arnsperger. Zur Lehre von. den sogenannten Dermoid Cysten des Ovarium, Virchow's Archiv, Bd. clvi., Heft 1, 1899.

9. J. G. Clark. Review of Bandler's article, Progressive Medicine, June, 1902, p. 223, "Origin of Dermoid Cysts."

10. Klein. Ueber die Combination von Dermoidcysten mit anderen Geschwultstformen des Ovarium, Inaug. Diss. Freiburg, Bd. i., 1893.

11. Niemer. Ueber die Combination von Kystoma und Dermoid Cyste des Ovarium, Inaug. Diss., Greifswald, 1895.

12. Simmerling. Cited by Pfannenstiel in the following: J. Pfannenstiel, Ueber die Pseudomucine der cystischen Ovarientumoren, Archiv f. Gynäk, Bd. xxviii. p. 442.

13. J. Pfannenstiel. Ueber die Histogenese der Dermoidcysten und Teratome des Eierstocks, Centralblatt f. Gynäk, 1897, No. 25, p. 799.

14. M. Wilms. Deutsche Zeitschrift f. Chirurgie, 1898, Bd. xlix., Heft 1.

ADRENAL TUMORS.

By Paul G. Woolley, B.S., M.D.,
GOVERNORS' FELLOW IN PATHOLOGY, M'GILL UNIVERSITY.

(From the J. H. R. Molson Laboratory of Pathology, McGill University, Montreal, Canada.)

Although the literature on the subject of adrenal tumors is not an extensive one, it has seemed to me that it would be useful to collate it, and so render it more accessible to students, for it is a scattered one. Such a collation will be based upon the paper of Kelynack, which up to its time was the most useful and comprehensive one in existence. Since the time of its publication many new facts have been added to our knowledge of these tumors, and especially to our knowledge of the malignant growths, which makes it necessary to add to the above-mentioned paper, admirable as it is.

Writers on pathology have not, apparently, been impressed by the remarkable facts discovered in the peculiar tumors in these important organs, for the current text-books—English and German alike—mention few of the common or uncommon features of them. One reason for such a neglect is that the earlier, and the later writers, too, have been interested in the relation between changes in the adrenal glands and Addison's disease, with the result that the case reports are of little or no present value in a large number of cases. There are, however, a few papers which are of much importance in this connection, notably those of Rolleston and Marks, Ramsey, Kelly, and Jores.

In discussing adrenal tumors I shall first deal with the benign tumors and then with the malignant ones.

Benign Tumors. The benign tumors of the adrenals belong in by far the greater number of cases to one class, namely, the adenomata, but the following varieties have also been reported: fibromata, lipomata, neuromata, gliomata, angiomata, and cystomata.

Fibromata have been reported by Saviotti and Mattei, but there is some doubt as to the authenticity of the cases, the general opinion being that they are, in all probability, fibro-adenomata—a class of tumors which is very common, and in which any proportion may exist between fibrous tissue and parenchyma. Fibromata may, however, occur, but are very rare.

Lipomata likewise have been reported—notably one case by Byford—but here, too, the probability is that these cases are tumors simulating lipomata, but in reality being adenomata which have undergone extreme fatty degeneration—a process which is extremely common in the adrenal and especially so in the adenomatous tumors.

Gliomata have been recorded in the literature by Virchow and Marchand. Reports coming from such sources are to be looked on as

valuable; but if such tumors do occur they must be rare anomalies, and due to tissue misplacement, for at the present time there is no reason to suspect that the adrenals contain any epidermic elements which could give rise to gliomatous tumors. Indeed, it has been very clearly shown in the past year that the old idea that the medulla of the adrenal was a derivative of nervous tissue is entirely erroneous, and that ganglionic tissue takes no part in the organogenesis.

Neuromata are to be looked upon with much suspicion, and although several cases have been reported by Weichselbaum, Armanni, and Formad, it is a question whether these are not really cases that should be classed as fibromata. If there is an authentic case of neuroma of the adrenal it must be an excessively rare one, and must be derived from one of the ganglia near the gland.

Of the more complex tumors there are three general classes, namely, adenomata, cysts, and angiomata, and in this last class are included two varieties—hæmangiomata and lymphangiomata.

Adenomata in general belong in two categories as regards size and multiplicity in the same organ. The most common are the small multiple adenomata, the large single tumors being far less commonly seen.

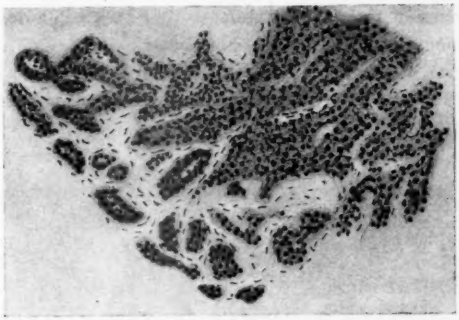
The small adenomata appear as yellowish nodules varying in size from a mustard-seed to a small pea. They occupy the medulla and the cortex, and are occasionally found just outside of the cortex, but beneath the capsule. In other words, they may arise in any zone of the organ.

When these are examined microscopically they are seen to be composed of cells which appear like adrenal cells affected by an advanced grade of fatty degeneration.

The larger adenomata—which occur singly, but occasionally bilaterally—show in their simpler forms a structure similar to that of the small adenomata, and their cells show the same tendency to fatty change. They usually originate in the cortex of the organ, and while they may form large tumors, they never involve the whole gland, and are usually seen as nodules projecting above the surface of the organ which they occupy. Their structure is more complicated than that of the small adenomata, and the arrangement of their columns of cells may become very intricate, as is the case in any other adenomatous tumor. As they increase in size the cells in the centre of the tumor undergo more or less fatty degeneration, and this process may extend to the supporting tissues, until the centre breaks down to form a cyst with mushy contents, or hemorrhage occurs into the softened tissue, forming a hemorrhagic cyst. By a gradual increase in the hemorrhage a huge cyst may at length be produced, similar to the one reported by Pawlik, which contained 10 litres of bloody material. In such a way, I believe, all the blood cysts of the adrenals arise, for hemorrhage into these

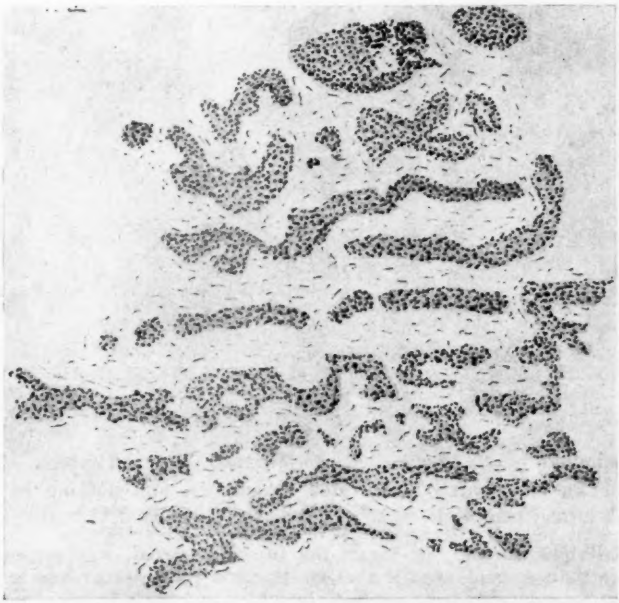
adenomata, and indeed into the glands themselves, is not a remarkably uncommon occurrence.

FIG. 1.



Case of cystic fibro-adenoma of adrenal. Zona glomerulosa in the wall of the tumor. Leitz eye piece IV., ocular 3. (Camera lucida.)

FIG. 2.



Zona fascicularis in wall of the tumor. Same magnification.

But besides these degenerative changes others may occur, and the resulting tumors have furnished the occasion for the reports of Letulle and Pilliet on "Surrénalites Nodulaires Hyperplastiques" and "Scléroses." In these so-called hyperplastic tumors there has apparently been an increase of the fibrous tissue, so that they come under the head of fibro-adenomata of more or less well-marked types.

The features of such tumors will be most easily remarked, I think, if I describe in some detail a tumor which came into my hands through

FIG. 3.

Zona reticularis in wall of tumor. Same magnification.

the kindness of Dr. McCrae, of the Montreal General Hospital. The tumor was accidentally discovered at autopsy, and nothing in the man's history can be shown to be due to the presence of the tumor.

The right adrenal, in which the tumor occurred, was somewhat larger than normal, even if the growth could be neglected, and at one end appeared a rounded protuberance, which was fairly firm and rather elastic. On section the gland itself was apparently normal. The

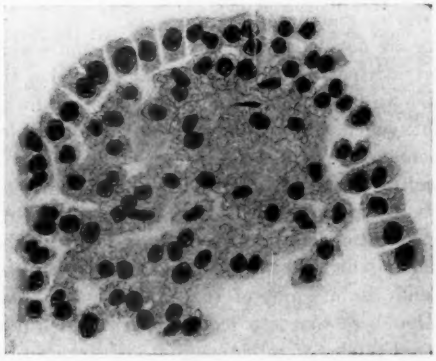
tumor, on section, presented a peculiar appearance. It was partially cystic, its contents being dark-brownish material, rather granular in appearance. The walls of the cyst were yellowish, with dark striations,

FIG. 4.

Areas of infiltration with lime salts. Leitz E. I., ocular 4.

and firm and tough. At one place there was an area that had the appearance of and cut like cartilage. To the apex of this area, which

FIG. 5.



Portion of a column of adrenal cells from zona fascicularis. Leitz E. IV., ocular 6. (Camera lucida.) The stain in all cases has been carbol-thionin.

projected into the cyst, was attached an arborescent mass of tissue, generally quite dark in color, which had the appearance of an intracystic papilloma.

On section of the wall of the cyst it was at once remarked that inside a compressed layer of fairly normal gland cortex was a fibroid and œdematous layer, composed of masses and columns of gland cells separated by masses of œdematous fibrous tissue, with occasional areas of pigmented material (the remains of old hemorrhage) and a few patches of calcareous deposit. (Figs. 1 to 5.) The area which had appeared like hyaline cartilage proved to be simply a hyaline fibrous tissue with a few nuclei, while the papillary, arborescent mass was the remnant of gland tissue which had not completely degenerated, and which had remained attached to fibrous strands and filled between with hemorrhagic detritus. This cystic fibro-adenoma was the size of a small English walnut.

Besides the hemorrhagic cysts two other varieties have been reported, namely, a serous variety by Ogle and a hydatid cyst by Bennett. This last, however, is a doubtful case, for in the description there are no details that would positively identify it.

Angiomata are rather rare growths, if we consider simply the benign forms, Klebs, Laboulbene, Vogel, and Seltz having reported cases. The case of Payne was a blood vascular tumor, while those mentioned by the other authors were lymphangiomata. They present no unusual features.

Malignant Tumors. When we come to study the primary malignant tumors of the adrenals we find a rather anomalous group of new-growths. The peculiarities of these tumors depend primarily upon the fact that they have their origin in a tissue that is less stable than epithelium or hypothelium, and which has been differentiated at a comparatively recent time, histogenetically, from the middle germ layer, and which is more closely related to the supporting tissues than are the two covering membranes of the body.

The adrenals are developed from the peritoneum—which in its turn has been a derivative of the middle germ layer—and of that division of mesoderm which we call mesothelium. This mesothelium seems to be the origin of tumors which at one time corresponded morphologically to the class of carcinomata, at another to sarcomata, and at another of a group of tumors which present a likeness to both the above types either in the same or in different nodules. Such tumors various authors have described in too little detail, and one such has furnished me with a text for a paper in which I have discussed at some length the changes which occur and the meaning of these variations. It will, therefore, suffice to mention here that the feature of greatest interest is the tendency for adrenal tumors of carcinomatoid appearance to form nodules, which may be purely sarcomatous or sarcocarcinomatoid, as the case may be. Rolleston and Marks and others emphasize this point.

As types of malignant tumors originating in the adrenals the following have been mentioned: carcinomata, sarcomata, endotheliomata, and peritheliomata.

In looking over the literature I have been unable to satisfy myself that the latter two varieties exist, although I have specimens of an aberrant adrenal tumor of the kidney that was distinctly a perithelioma; so these may exist also in the adrenal itself. If they do occur, and if they have the characteristics of the aberrant tumor that I have seen, they are tumors which show the ordinary characteristics of the malignant vascular tumors.

The other malignant tumors of the adrenals fall into two classes as they are described—*i. e.*, sarcomata and carcinomata. This classification rests, of course, on purely morphological grounds—a basis which is absolutely inadequate, White to the contrary notwithstanding—for many reasons, which I have discussed and which are sufficiently obvious. In my paper I described the tumor that I was studying as mesothelioma.

These adrenal mesotheliomata—or mesolepidomata, as Adami calls them—occur as large or small tumors, circumscribed or infiltrating, and originate in one of the zones of the cortex of the adrenal gland. When circumscribed they metastasize chiefly by the bloodvessels, but also by the lymph vessels in a certain number of cases. When they are infiltrating they may involve any of the neighboring organs, chiefly the liver and kidney, and are especially prone to invade the inferior vena cava. When small they may give rise to no symptoms that aid diagnosis, but they may give rise to many and serious symptoms by their metastases. The larger tumors produce various symptoms of tumor—such as a palpable, movable, or fixed mass in the renal region—and especially to symptoms of venous obstruction, due to pressure on, or thrombosis of, the vena cava. Metastasis, as a rule, occurs by the bloodvessels, and is most common in the liver and lungs. In twenty-two cases which I have collected from the literature which can be called carcinomata by the postulates of Rolleston and Marks there were metastases, as follows:

Liver	13 times.	Pericardium	1 time.
Lungs	11 "	Endocardium	1 "
Lymph glands	7 "	Uterus	1 "
Brain	3 "	Ovary	2 times.
Kidney	2 "	Spleen	1 time.
Peritoneum	3 "	Bones	2 times.
Appendix	1 time.	Diaphragm	1 time.
Stomach	1 "	Bladder	1 "
Mesentery	1 "		

These tumors occur at all ages. The youngest was nine months (Cohn) and the oldest seventy-three years (Ritchie and Bruce). In Ramsey's list of thirty-seven carcinomata[1] twenty-two were in men,

[1] It will be seen from these figures that Ramsey has given a longer list of primary carcinomata than I. This is because I do not feel that many of the cases quoted by him are primary, as judged by the rules of Rolleston and Marks, which I think are very useful and very logical, considering that "judgment is difficult."

and in my list of twenty-two, eleven were in men. I shall append a table of the cases of the carcinomatoid tumors judged by the postulates of Rolleston and Marks.

The microscopic appearances of the malignant adrenal tumors vary. I have seen none that show purely sarcomatous appearances, but, judging by some of the descriptions in the literature, they do occur. Indeed, they are the more common variety. They conform in appearance to other sarcomata, and are spindle-celled or round-celled in type. The carcinomatoid tumors have an alveolar appearance corresponding in a certain extent with the arrangement of the normal gland. In some instances they have a peculiar perivascular arrangement, which I think is uncommon.

The primary tumor may correspond to the carcinomata even in the arrangement of the reticulum, but there is a tendency for the reticulum to become intercellular even when in the larger part of the tumor it surrounds groups of cells. In the case which I described the reticulum in the primary tumor separated groups of cells, while in the metastases, in lymph glands, and brain it was intercellular. In the lungs the arrangement took on characters of the so-called carcinoma-sarcomatodes. The origin of these tumors has been shown to be, at least in some cases, in the parenchyma of the organs, and is not due to connective-tissue changes or to proliferation of the cells of the bloodvessels.

Finally, the cells of malignant adrenal tumors, like those of other malignant growths, are larger as a rule, the nuclei are larger comparatively, the protoplasm less in amount, and the nuclear substance more abundant than normal. Mitotic figures, regular and atypical, are common.

The most noticeable feature in these tumors is their well-marked tendency to variation in type, due to the remarkable inclination of the cells to metaplastic changes.

In the accompanying tabulation of the primary carcinomatoid adrenal tumors there will be found a brief epitome of the characters and clinical observations abstracted from the case reports. In the tabulation I cannot include the cases of Stybr and Nuno Porto, because I have not been able to read the first or obtain the second paper, and because I have been unable to find any adequate abstract of either case. It has, however, been asserted by several authorities that the first was a primary melanotic carcinoma, and that the second was also a primary growth.

Secondary Malignant Growths. Secondary tumors are not uncommon, and occur in persons past middle life in the great majority of cases. In looking over the autopsy records of the Royal Victoria Hospital I was able to find mention of secondary sarcoma in one case in fifteen; of secondary carcinoma in seven cases in forty-eight.

The case of sarcoma occurred in a case of multiple sarcoma, and nodules were found in both adrenals. The cases of carcinomata occurred as follows: cancer of the stomach with metastases in the left adrenal, three times; in the right adrenal, twice; cancer of the pancreas, in both adrenals, once; cancer of the bile-duct, in both adrenals, once; in the left, once; cancer of the intestines, in the right adrenal, once.

NOTE.—Since I have had the proofs of the preceding remarks, I have come across three interesting papers that had escaped my notice, in spite of my care in searching the literature.

One of these papers is that of Morris (*Brit. Med. Journ.*, 1899, vol. ii. 1336), which discusses three cases of adrenal growths, all of which the author considers to be sarcomata, although, as he says, the resemblance to carcinoma is a very marked feature in some cases of the growths. The first case has been recorded in the *Reports of the Middlesex Hospital* (1888, p. 230) as a "Sarcoma of the Adrenal." It occurred in a man, aged fifty-one years, and weighed 61½ ounces. The left adrenal only was involved. His second case was in a man, aged forty-three years, and in this instance the tumor was on the right side. No autopsy was obtained, and there is some doubt as to whether the growth was certainly primary in the adrenal.

The third case was that of a woman, aged forty-three years. In this case the growth was a cystic sarcoma, and after operation the patient died, with recurrences.

The second paper is that of Orr (*Edin. Med. Journ.*, 1900, vol. l.), who reports a case of sarcoma in a child, aged seven weeks. Both adrenals were affected. The liver was involved by the growth. Dr. Leith gives a good pathological discussion of the findings, and decides that the case is one of small round-celled sarcoma, although it could be distinguished only with some difficulty from carcinoma. This is the youngest case on record.

Three of these cases then deserve to be classed with the so-called "primary sarcomata," the other is possibly primary.

The third paper is that of Schnittenhelm (*Wien. klin. Rundschau*, 1901), and in this paper a case of medullary cancer of both adrenals in a man, aged fifty-five years, is described. This case may be one of primary carcinoma. The remarkable features of this case are the clinical symptoms, which Schnittenhelm ascribes to an auto-intoxication. There was no pigmentation.

TABLE OF PRIMARY CARCINOMATOID ADRENAL TUMORS.

No.	Source.	Publication.	Sex and age.	Gland.	Nature.	Secondary growths.	Pigmentation.	Remarks.
1	Rolleston and Marks,	Amer. Journ. Med. Sci., n.s., vol. cxvi. p. 116.	Male, 50	Left.	Round-cell carcinoma.	Liver, peritoneum.	None.	Ascites; œdema of feet. Diagnosis: abdominal aneurism.
2	Ibid.,	Ibid.	Male, 40	Right.	Round-cell carcinoma.	Right and left lungs, liver, aortic glands.	None.	Pneumonia.
3	Ibid.,	Ibid.	Female, 52	Right.	"Malignant adenoma."	Liver.	None.	Anæmia; leucocytosis; emaciation; enlarged liver and spleen; kidney invaded; pleural effusion; ascites; œdema of legs.
4	Ogle,	Trans. Path. Soc., London.	Female, 3	Left.	"Malignant adenoma."	Liver.	"Gypsy color."	Constant vomiting; weight increased; pubic hair, moustache; colon depressed.
5	Ritchie, Bruce,	Edinburgh Med. Journ.	Male, 73	Both.	Carcinoma.	Lungs.	None.	Vomiting.
6	Weinburg, Turquet,	Bull. Anat. Soc., Paris.	Female, 36	Both.	Carcinoma.	Both lungs, cerebellum, appendix.	.....	Dilated stomach; diarrhœa; lumbar pain; vomiting; severe headache.
7	Fenwick,	See Rolleston and Marks.	Male, 62	Right.	Carcinoma.	Liver, mesentery, stomach; pancreas invaded by continuity.	None.	Pulsation (not expansile); left adrenal enlarged; vena porta and vena cava inferior thrombosis; six ounces of blood clot in tumor; blood-stained fluid in peritoneal cavity.
8	Brooks,	Redcliffe Infirmary.	Female, 49	Left.	Carcinoma.	Liver, lungs, right adrenal, bronchial glands.	None.	Irregular temperature; emaciation; pain down left leg.
9	Ibid.,	Roy. Col. Surg. Museum.	Female, 32	Right.	Carcinoma.	Liver and aortic lymph glands.	.....	Growth into vena cava inferior; hypertrichosis.
10	Carrière Délearde,	Arch. de Méd. Expér.	Male, 54	Both.	"Epithelieme atypique."	Liver, lungs.	None.	Palpable tumor; œdema of legs; cachexia; diarrhœa; pleural effusion; ascites.
11	Pawlik,	Arch. f. klin. Chirurgie.	Female, 50	Both.	Melanotic carcinoma.	Right kidney, brain, lungs, pleuræ, epicardium, endocardium, peritoneum, liver, and uterus.	.....	Extension of right kidney; loss of appetite; vomiting; increased urine; right facial paralysis; right pupil dilated; almost complete amnesia; right hemiplegia; urine and feces passed involuntarily.

12	Bruchanow,	Zeits. f. Heilkunde.	Female, 14 mos.	Right.	Medullary carcinoma.	Lymph glands, right ovary.	.....	Thrombosis inferior vena cava; œdema of feet; extension to liver.
13	.....	.....	Male, 63	Right.	Carcinomatous degeneration of a struma.	Liver and right lung; lymph glands.	.....	Extension to liver; œdema of feet; asthenia.
14	.....	....	Female, 66	Right.	Cancer.	Lymph glands; spleen.	.....	Growth in kidney a collateral development in accessory gland.
15	Orth,	Arbeiten Göttingen.	Female, 4½	Right.	Carcinoma.	Liver and lungs.	.....	Abnormally developed genitalia.
16	.....	....	Male, 49	Left.	Carcinoma.	Liver.	.....	Death from marasmus.
17	Marchand,	Virchow's Festschrift.	Female, 20	Right.	Carcinoma.	Left ovary, liver.	.....	Irregular menstruation; œdema of legs.
18	Collinet,	Bull. Anat. Soc., Paris.	Male, 53	Right.	Epithelioma.	Diaphragm, reno-cæcal ligament.	None.	Œdema of legs; loss of appetite; growth extended to liver and kidney; cells in portal vein.
19	Stoukoventoff,	Gaz. Méd. de Paris.	Female, 50	Both	Carcinoma.	Liver and lungs.	None.	Fever; pain over liver; liver enlarged; sanguineous expectoration; œdema of legs; albuminuria; dyspnœa; cyanosis.
20	Posselt,	Wien. klin. Woch.	Male, 46	Left.	Carcinoma.	Left lung, kidney, lumbar vertebræ.	Present.	Had pulmonary tuberculosis and Addison's disease; symptoms of these.
21	Kelly,	Ziegler's Beiträge.	Male, 68	Left.	Carcinoma.	Bladder and lungs.	.....	Metastasis by inferior vena cava.
22	Woolley,	Journ. Exp. Medicine.	Male, 42	Both.	Mesothelioma.	Right lung, brain, lymph glands.	None.	Fainting attacks; weakness; dyspnœa; incontinence of urine and feces; symptoms of meningitis; frontal headache; vomiting; optic neuritis.

LITERATURE.

PRIMARY CARCINOMATA.

Kelly. Ziegler's Beiträge, 1898, vol. xxiii. p. 280.
Posselt. Wien. klin. Woch., 1894, p. 630.
Stoukoventoff. Gaz. Méd. de Paris, 1895, vol. xlix. p. 581.
Rolleston and Marks. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1898, n. s., vol. cxvi. p. 383.
Carrière et Delearde. Arch. de Méd. Exp., 1900, vol. xii. p. 28.
Pawlik. Arch. f. klin. Chir., 1896, vol. liii. p. 530.
Orth. Berlin, 1893, pp. 41–75.
Marchand. Intern. Beitr. z. Wissensch. med. Festschrift, 1891, vol. i. p. 3.
Collinet. Bull. Soc. Anat., Paris, 1892, p. 325.
Ritchie and Bruce. Edinburgh Medical Journal, 1890, vol. xxxvi. p. 12.
Weinburg et Turquet. Bull. Soc. Anat., Paris, 1897, p. 751.
Bruchanow. Zeitschr. s. Heilkunde, Bd. xx.
Hausmann. Berl. klin. Woch., 1876, vol. xiv. p. 465.

SECONDARY CARCINOMATA.

Peacock and Bristowe. Trans. Path. Soc., London, 1856, vol. viii. p. 333.
Peacock and Bristowe. Ibid., p. 337.
Leva. Arch. f. Path. Anat., 1895, vol. cxxxv. p. 35.
Gibbs. Trans. Path. Soc., London, 1856, vol. viii. p. 255.
Wigglesworth. Liverpool Med. Chir. Journ., 1892, vol. xii. p. 254.
Nuno Porto. Med. Contemp., Lisbon, 1884, vol. xi. p. 188.
Sapalier. Bull. Soc. Anat., Paris, 1881, vol. lvi. p. 264.
Heitler. Wien med. Presse, 1875, vol. xvi. p. 809.
Döderlein. Inaug. Diss., Erlangen, 1860.
Sibley. Trans. Path. Soc., London, 1858, vol. x. p. 272.
Stybr. Sborn. lék. v. Praza, 1890, vol. iv. p. 84.
Jeaffreson. Trans. Path. Soc., London, 1867, vol. xix. p. 428.
Bristowe. Ibid., p. 415.
Schuchardt. Bresl. Arztl. Zeits., 1883, vol. v. p. 181.
Cayley. Trans. Path. Soc., London, 1864, vol. xvi. p. 250.
Murchison. Ibid., 1857, vol. ix. p. 400.
Murchison. Ibid., 1867, vol. xix. p. 416.
Hadden. Ibid., 1885, vol. xxxvii. p. 515.
Haldane. Edinburgh Med. Journ., 1861, vol. vii. p. 586.
Lubet-Barbon. Bull. Soc. Anat., Paris, 1885, vol. lx. p. 136.
de Ruyter. Langenbeck's Arch., 1890, vol. xl. p. 98.
McGillivray. Austral. Med. Journ., 1868, vol. xiii. p. 294.
Arnott. Trans. Path. Soc., London, 1867, vol. xix. p. 418.
Fleiner. Berl. klin. Woch., 1889, No. 51, p. 1101.
Ball. Bull. Soc. Anat., Paris, 1857, vol. xxxii. p. 85.
Besnier. Ibid., 1850, xxxii. p. 85.
Troisier. Bull. et Mém. Soc. Méd. Hôp. de Paris, 1890, 4 s., vol. vii. p. 266.
Greenhow. Trans. Path. Soc. London, 1865, vol. xvii. pp. 303, 310–331.
Greenhow. Ibid., 1866, vol. xviii. p. 260.
Greenhow. Ibid., 1872, vol. xxiv. p. 238.
Kernig. St. Petersburg med. Woch., 1888, n. f. v. p. 63.
Ogle. Trans. Path. Soc., London, 1864, vol. xvi. p. 250.
Addison. On the Constitution and Local Effects of Diseases of the Suprarenal Capsules. London, 1855.
Ball. Bull. Soc. Anat., 1858, vol. xxxiii. p. 423.
Da Costa. Proc. Path. Soc., Philadelphia, 1857, vol. i. p. 153.
Delpierre. Gaz. des Hôp., 1856, p. 393.
Mettenheimer. Deutsche klinik., 1856, p. 483.
Duclos. Bull. Gén. d. Thérap. Méd. et Chir., 1863, vol. lxiv. p. 97.

SARCOMATA.

Ramsey. Johns Hopkins Hospital Bulletin, 1899, p. 20.
Affeck and Leith. Edinburgh Hospital Report, 1896, vol. iv. p. 278.

Jores. Deutsche med. Woch., 1894, p. 208.
Fränkel. Virchow's Arch., vol. ciii. p. 244.
Lubarsch. Ibid., 1894, vol. cxxxv.
Dobberton. Ziegler's Beiträge, vol. xxviii. p. 46.
Fox. Trans. Path. Soc., London, 1894, vol. xxxvi. p. 460.
Greenhow. Ibid., 1866, vol. xviii. p. 260.
West. Ibid., 1878, vol. xxx. p. 419.
Blackburn. Journ. Amer. Med. Assoc., 1888, vol. x. p. 389.
Pilliet. Bull. Soc. Anat., Paris, 1888, vol. lxiii. p. 716.
Orth. Arbeiten aus der Path. Inst., Göttingen. Berlin, 1893, pp. 41–75.
Berdach. Wien. med. Woch., 1889, vol. xxxix. pp. 357, 385.
Cohn. Berl. klin. Woch., 1894, p. 266.
Kussmaul. Wurtz. med. Zeits., 1863.
Smith. Dublin Journ. Med. Sci., 1876.
Meckel. Ziemssen's Handb. der Spec. Path. u. Ther., New York, 1878, vol. viii.
Rosenstein. Virchow's Arch., 1881, lxxxiv. p. 322.
Cade. Fort. Norske Med. Selsk i. Kristiania, 1886.
Perry. British Medical Journal, 1898, p. 1382.
Lazarus. Medical Press and Circular, London, 1894, p. 467.
Turner. Trans. Path. Soc., London, 1884, vol. xxxvi. p. 464.
Schwarz. Bull. et Mém. de la Soc. de Chir., Paris, 1893–94, p. 764.
Ambrosius. Il Morganni, 1891, No. 8.
Eberth. Arch. f. Path. Anat., 1881, vol. liv. p. 21.
Griffiths. British Med. Journ., 1889, p. 242.
Burghart. Berlin. klin. Woch., 1897, p. 259.
Caillé. Arch. Pediatrics, New York, 1895, vol. xii. p. 594.
Earle. Journ. Amer. Med. Assoc., 1894.
Maukiewicz. Diss., Strasburg, 1887.
Martin. Lyon Médicale, July, 1896.
Scharago. Meditsina, St. Petersburg, 1893, vol. v. pp. 82, 98.
Le Count. Trans. Chicago Path. Soc., 1902, vol. v. p. 67.

ADENOMATA.

Pilliet. Bull. Soc. Anat., Paris, 1889, vol. lxiv. p. 199.
Pilliet. Ibid., p. 423.
Pilliet. Ibid., 1892, 5me. ser., vol. vi. p. 573.
Letulle. Ibid., p. 334.
Horn. Virchow's Arch., 1891, vol. cxxvi. p. 191.
Beneke. Ziegler's Beiträge, 1891, vol. ix. p. 440.
Kelly. Ibid., 1898, vol. xxiii. p. 280.
Cayley. Trans. Path. Soc., London, 1865, vol. xvi. p. 246.
Cayley. Ibid., 1868, vol. xix. p. 246.
Turner. Ibid., 1885, vol. xxxvi. p. 459.
Moxon. Ibid., 1869, vol. xx. p. 385.
Berdez. Arch. de Méd. Expt., 1892.
Byford. Obstet. Gaz., Cincinnati, 1889, vol. xii. p. 84.
Di Mattei. Gior. d. r. Accad. di Med. di Torino, 1881, 3 s., xxxiv. p. 127.
Kelynack. Journ. of Anat. and Phys., 1896, vol. xxx. p. 539.
Kelynack. Edinburgh Med. Journ., 1897, p. 263.
Letulle. Bull. Soc. Anat. de Paris, 1888, vol. lxiii. p. 302.
Letulle. Gaz. hebd. de Méd., Paris, 1892, 2 s., vol. xxxix. p. 306.
Sutton. Tumors, Benign and Malignant, London, 1893, p. 98.
Weinberg. Bull. Anat. Soc., Paris, 1895, vol. lxx. p. 628.
Beadles. Trans. Path. Soc., London, 1898, vol. xlix. p. 260.
Ogle. Ibid., 1865. vol. xvi. p. 252.
Ogle. Ibid., 1868, vol. xix. p. 252.
Rayer. L'Éxperience, 1837.
Pawlik. Arch. f. klin. Chir., 1896. vol. liii. p. 582.
Bennet. Trans. Path. Soc., London, 1864, vol. xv. p. 224.
Carrington. Ibid., 1885, vol. xxxvi. p. 454.
Morris. London, 1901, vol. ii. p. 15.
Christie. Med. Times and Gaz., London, 1856, n. s., vol. xiii. p. 247.
Floersheim et Ouvray. Bull. Soc. Anat., Paris, 1895, p. 73.

NEUROMATA AND GLIOMATA.

Armanni. Monimento Napoli, 1874, vol. vi. p. 533.
Marchand. Virchow's Festschrift, 1891, vol. i. p. 3.
Formad. Trans. Path. Soc., Philadelphia, 1884, vol. xi. p. 184.
Virchow. Die Frankhafte Geschwülste, Berlin, 1862-65.

GENERAL LITERATURE ON ADRENAL TUMORS.

Neusser. Die Erkrankungen der Nebennieren, Wien, 1897.
Birch-Hirschfeld. Lehrbuch der Allgemeine Pathologie, 1877.
Averbeck. Die Addisonsche Krankheit.
De Paoli. Aniv. d. inseg. Chir. de F. Duranti u. Univ. di Roma, Rome, 1898, vol. i. p. 219.
Droubaix. Thèse de Paris, 1887.
Erni. Diss., Zurich, 1879.
Jonas. Annals of Surgery, 1898, vol. xxvii. p. 436.
Griffiths. British Med. Journ., 1889, p. 242.
May. Virchow's Arch., 1897, vol. cviii.
Rolleston. British Med. Journ., 1895.
Kelynack. Med. Chron., 1897, n. s., vol. viii. p. 401.
Bouchard. Traité de Pathologie Générale, Paris, 1895.
Féréol. Bull. Soc. Anat., Paris, 1857.
Gairdner. Monthly Journ. Med. Soc., London, 1850, vol. x. p. 382.
Habershon. Guy's Hospital Reports, 1866, vol. xii. 423.
Hamilton. Text-book of Pathology, London, 1894, vol. xi. p. 783.
Kiebs. Handbuch der path. Anat., 1876, vol. i. p. 580.
Lancereaux. Dictionnaire Encyclop. des Sci. Méd., Paris, 1875, 8s., vol. cxi., p. 161.
Leitenneur. Journ. de la Soc. Acad. d. l. Loire Inf., 1858, vol. xxxiii. p. 341.
Mattei. Gaz. hebdom. de Méd. et de Chir., 1864, p. 588.
Palarnidessi. Arch. Ital. di Chir. Med., Milano, 1895, vol. xxxiv. p. 80.
Payne. Trans. Path. Soc., London, 1869, vol. xx. p. 203.
Pye-Smith. British Medical Journal, 1887, vol. i. p. 99.
Laboulbène. Cited by Kelynack.

ON ADRENALIN GLYCOSURIA AND CERTAIN RELATIONS BETWEEN THE ADRENAL GLANDS AND CARBOHYDRATE METABOLISM.

BY C. A. HERTER, M.D.,

PROFESSOR OF PATHOLOGICAL CHEMISTRY, UNIVERSITY AND BELLEVUE MEDICAL COLLEGE, NEW YORK,

AND

A. J. WAKEMAN, PH.D.

THE adrenal gland was for the first time brought into relation with glycosuria by F. Blum,[1] of Frankfort, who in September, 1901, published observations showing that extracts of the adrenal glands of sheep are capable of inducing a slight or moderate grade of glycosuria when injected subcutaneously into dogs and rabbits. The results of Blum were confirmed in Europe, and led in this country to experiments with Takamine's adrenalin chloride and Abel's adrenalin which have extended our information as to the glycosuria following the administration of preparations made from the adrenals. Herter and Richards[2]

[1] Ueber Nebennierendiabetes, Deutsches Archiv für klin. Medicin, Bd. lxxi.
[2] Medical News, February 1, 1902.

found that the intraperitoneal injection of solutions of adrenalin chloride is followed almost regularly by the presence of large percentages of sugar in the urine, and the present writers made a study of some of the conditions under which adrenalin glycosuria occurs.[1] In this paper it is desired to offer a summary of the more important observations that have now been made, in the belief that they are of interest as throwing new light on the physiology of carbohydrate metabolism.

General Description of Experimental Adrenalin Glycosuria. The intensity and duration of adrenalin glycosuria depend in part on the mode of administration, in part on the size of the dose. Subcutaneous injections yield less sugar than intravenous or intraperitoneal injections. Direct applications to the surface of the pancreas usually cause considerable excretion of sugar, even when the quantity of adrenalin used is small (say 1 c.c. solution of adrenalin chloride 1 : 1000). The slightest glycosurias in proportion to the dose have come from the use of adrenalin chloride by the mouth. Dogs of medium size may receive 10 to 20 c.c. of the commonly used adrenalin chloride solution (1 : 1000) without developing glycosuria; larger doses may be followed by a moderate or considerable glycosuria. This relative inertness of the substance when given by the mouth has a certain practical importance, and is readily explained. Adrenalin is very easily oxidized, and quickly loses both its blood-pressure-raising property and its ability to induce glycosuria. When introduced into the stomach the gastric epithelial cells have an opportunity to destroy a considerable portion of the active substance before it is absorbed. It thus loses a large part of its efficacy in raising the blood pressure. It is preferable to give adrenalin subcutaneously to giving it by the stomach, for, in addition to securing greater precision and economy in dosage, this method has the advantage of avoiding any ill effects upon the stomach. We have never known the usual dose for subcutaneous use

[1] Table Showing Effect of Intraperitoneal Injection of Adrenalin of Dilution 1 : 1000.

Weight of dog.	Amount of solution used.	First catheterization after	Sugar.	Second catheterization after	Sugar.	
18.6 kilo.	9 c.c.	1 hour.	5.0 per ct.			
21 "	10 "	.....	1.0 "			
8.2 "	7 "	1 hour.	10.0 "			
11.3 "	10 "	1 "	5.3 "			
10.9 "	10 "	30 min.	5.0 "	1 hr. 30 min.	6.5 per ct.	
13.2 "	11.5 "	2 hr. 30 min.	5.0 "	3 " 10 "	7.33 "	
10 "	5 "	40 min.	6.11 "	2 " 20 "	11.5 "	
5 "	2 "	4 hours.	3.75 "			
6.8 "	10 "	.....	4.8 "			
8.2 "	5 "	.....	1.25 "			
7.3 "	5 "	.....	2.7 "			
7.3 "	10 "	1 hr. 25 min.	2.0 "	6 hr. 30 min.	4.2 per ct.	Abel's adrenalin.
6.4 "	10 "	1 " 10 "	7.15 "	.....	.....	" "

(0.3 to 1.2 c.c.) to occasion glycosuria, even when repeated at intervals of three or four hours.

The degree and duration of the glycosuria vary widely in different animals, and sometimes in the same animals at different times. Intraperitoneal injections of 5 c.c. of adrenalin chloride in normal dogs of medium size (8 to 15 kilos) almost without exception cause the appearance (within one or two hours) of a glycosuria, with from 3 to 10 per cent. of sugar in the urine. The duration of the glycosuria following a single dose is seldom longer than thirty hours. During this time there is a total excretion of glucose which does not commonly exceed 2 or 3 grammes. The amount of sugar which appears during and after frequently repeated doses of adrenalin may greatly exceed these amounts. For example, this is well shown in the following experiment, in which the pancreas was repeatedly painted with adrenalin:

Experiment. Normal dog; weight, 13.6 kilos; well nourished. Meat diet. Bladder emptied; urine normal. Lacteals found distended. Pancreas divided into two nearly equal parts. Adjoining duodenum also cut through transversely. Between 10.45 A.M. and 9.25 P.M. head end of the pancreas painted ten times with 1 c.c. adrenalin chloride solution (1 : 1000). Slightly under ether throughout the entire experiment.

Urine,	first	catheterization	12.35 P.M.,	70 c.c.,	7.25	per cent.	sugar.	
"	second	"	2.15 "	60 c.c.,	14.3	"	"	
"	third	"	3.15 "	48 c.c.,	12.5	"	"	
"	fourth	"	4.30 "	25 c.c.,	9.75	"	"	
"	fifth	"	5.50 "	14 c.c.,	6.0	"	"	
"	sixth	"	7.00 "	10 c.c.,	2.22	"	"	
"	seventh	"	8.00 "	6 c.c.,	1.82	"	"	
"	eighth	"	9.00 "	7 c.c.,	1.4	"	"	
"	ninth	"	10.15 "	4.5 c.c.,	0.83	"	"	

The total quantity of sugar excreted during this experiment was 23.4 grammes (estimated as glucose). The observation is instructive not merely in showing how high a grade of glycosuria may be caused by the action of adrenalin, but also as indicating how small a quantity of adrenalin is capable of calling forth so great an amount of sugar. The amount of adrenalin substance employed in this experiment was approximately 0.01 gramme. We do not know of any form of experimental glycosuria in which such pronounced effects can be obtained with so small a quantity of toxic material.

The susceptibility of different dogs to adrenalin varies considerably so far as glycosuria is concerned. One sometimes finds animals which do not show any glycosuria whatever, even after one or more applications to the pancreas.[1] The differences noted appear to be connected with the state of nutrition, and especially with the quantity of gly-

[1] Many of our animals showed themselves insusceptible to the action of piperidin in causing glycosuria, while others excreted very large quantities of sugar. This difference appeared to be largely independent of the size of the dose applied to the pancreas.

cogen which is stored in the organism. It appears doubtful, however, if these differences in susceptibility can be accounted for wholly in this way. It seems to us that there are other factors of which the nature is unknown.

In adrenalin glycosuria the sugar of the blood is regularly increased but falls rapidly with the decline in the sugar of the urine, and after a time may drop below the original normal level. In respect to the increase of blood sugar adrenalin glycosuria resembles the majority of cases of human diabetes, and differs from the experimental glycosuria after phloridzin, where the sugar-content of the blood is commonly lower than normal. The volume of the urine in adrenalin glycosuria is usually distinctly increased. The presence of diacetic acid or oxybutyric acid has not been observed. The occurrence of glycosuria from adrenalin is wholly independent of any change in the general blood pressure, as was shown in experiments where sugar occurred in the urine in spite of a marked fall in carotid blood pressure from nitroglycerin.

Physiological Characters of Adrenalin Glycosuria. One of the first questions that arises relates to the origin of the sugar which appears in the urine. This sugar might be thought of as coming either from an increased conversion of hepatic glycogen or from a diminished combustion of sugar. In favor of the former view are two facts—first, the decline in the glycogen store of the liver during adrenalin glycosuria; and, secondly, the increased sugar-content of the blood of the hepatic vein as compared with the blood of the portal vein. The following table gives three typical observations made by Dr. Richards upon the sugar of the blood of the femoral artery, portal vein, and hepatic vein, before and after treatment of the pancreas with adrenalin. The collections of blood were made simultaneously by means of specially designed canulæ.

These figures call for little comment. In two of the three observations the sugar of the blood of the femoral artery, portal vein, and hepatic vein showed a fairly close correspondence before the application of adrenalin. In the third case the blood sugar of the hepatic vein was considerably lower than that of the blood of the portal vein. In all three cases the percentage of blood sugar of the hepatic vein rose quickly to a point in excess of the percentage in the portal vein, and remained so during the subsequent observations. It is safe to infer that this behavior of the blood sugar is referable to the increased production of sugar within the liver.

TABLE SHOWING PERCENTAGE OF SUGAR IN BLOOD BEFORE AND AFTER TREATMENT OF PANCREAS WITH ADRENALIN.

Weight of dog.	Starved.	Blood drawn at	Pancreas painted at	Sugar in blood from		
				Femoral artery.	Portal vein.	Hepatic vein.
8.2 kilo.	48 hours.	3.50 P.M.	.....	0.142 per ct.	0.148 per ct.	0.143 per ct.
		.....	4.04 P.M.			
		4.08 P.M.		0.191 "	0.151 "	
		4.21 "		0.179 "	0.154 "	0.177 "
		5.07 "		0.132 "	0.107 "	0.130 "
9.2 kilo.	24 hours.	4.23 P.M.	.....	0.160 per ct.	0.165 per ct.	0.164 per ct.
		.....	4.39 P.M.			
		4.49 P.M.		0.247 "	0.197 "	0.284 "
		5.20 "		0.322 "	0.245 "	0.346 "
7.8 kilo.	20 hours.	4.21 P.M.	.....	0.159 per ct.	0.169 per ct.	0.136 per ct.
		.....	4.40 P.M.			
		4.44 P.M.		0.187 "	0.167 "	0.201 "
		5.06 "		0.215 "	0.187 "	0.252 "
		4.46 "		0.208 "	0.207 "	0.209 "

In what way adrenalin occasions an excessive conversion of glycogen into sugar is still undecided, but there are some experimental observations that have to be considered in any attempt to form a judgment on this question. One of these is that applications of small amounts of adrenalin to the surface of the pancreas or injections into its substance have given rise to a more pronounced glycosuria than similar procedures in the case of the brain, liver, spleen, or kidney.[1] This suggests that in the production of glycosuria adrenalin acts especially, if not exclusively, upon the cells of the pancreas; but it has been impossible to prove that the action of adrenalin depends wholly on the presence of the pancreas, for total extirpation of this gland is quickly followed by an excretion of sugar.[2] Another difficulty arises from the fact that since adrenalin acts when introduced into the circulation, the substance may find its way to other organs when applied to the surface of the pancreas. If, however, it could be shown that there are substances which are capable of inducing glycosuria when painted on the pancreas, but do not cause it when introduced into the circulation or into the brain, spleen, or liver, we should have strong evidence that the substances in question when applied to the pancreas act on this organ only. A substance of this nature is potassium cyanide. The action of this poison in its relation to glycosuria is illustrated by the following tables:

[1] No observations of this kind have as yet been made upon the adrenal bodies.

[2] It is possible that some information could be obtained after total extirpation of the pancreas by making intraperitoneal injections of adrenalin when the quantity of sugar excreted from hour to hour is small and fairly constant.

TABLE SHOWING EFFECT OF APPLYING POTASSIUM CYANIDE SOLUTIONS TO PANCREAS.[1]

Weight of dog.	How applied to pancreas.	Amount of solution used.	Strength of solution.	Duration of application.	First catheterization after	Volume of urine.	Sugar.	
.....	Painted.	2 c.c.	$\frac{N}{1000}$	.....	1 hour.	.....	2.1 %	
4.5 kilo.	Painted.	3 "	"	30 min.	1 h. 40 m.	2 c.c.	'strong'	
6.8 "	Painted and injected.	2 "	"	10 "	1 hour.	9 "	0	
9.5 "	Painted and injected.	2 "	"	.....	30 min.	.....	6.0 %	Applicati'n to tail of pancreas.
7.2 "	Painted.	1.5 "	"	18 min.	2 hours.	5 "	1.5 %	
9.1 "	Injected.	3 "	"	.....	2 "	4 "	trace.	
11.8 "	Painted and injected.	3 "	"	10 min.	1 hour.	9 "	0	
10.4 "	Injected.	3 "	"	10 "	2 h. 45 m.	65 "	0.25 %	Applicati'n to head of pancreas.
6.8 "	Painted and injected.	2 "	"	10 "	2 hours.	8 "	trace.	
5.4 "	Painted and injected.	2 "	"	.....	4 h. 45 m.	7 "	trace.	

TABLE SHOWING EFFECT OF INTRODUCING POTASSIUM CYANIDE SOLUTIONS INTO A MESENTERIC VEIN OR INTO THE FEMORAL VEIN.

Weight of dog.	Where injected.	Amount of solution injected.	Strength of solution.	Duration of injection.	First catheterization after	Volume of urine.	Sugar.
9.1 kilo.	Into mesenteric vein.	3 c.c.	$\frac{N}{1000}$	.....	1 h. 10 m.	.....	0
10 9 "	" "	6 "	"	.....	.....	.....	0
6.8 "	" "	10 "	"	2 min.	2 hours.	13 c.c.	0
4.5 "	" "	14 "	"	2 "	2 h. 15 m.	35 "	0
8.2 "	" "	250 "	"	60 "	2 h. 10 m.	0	
7.7 "	" "	85 "	"	.....	2 h. 15 m.	23 c.c.	0
7.3 "	Into femoral vein.	5 "	"	25 min.	2 hours.	5.5 "	0
7.7 "	" "	3 "	"	30 "	2 hours.	12 "	0
9.1 "	" "	6 "	"	15 "	1 h. 30 m.	25 "	0
7.3 "	" "	200 "	$\frac{N}{100}$	.....	.....	.....	0
6.4 "	" "	200 "	$\frac{N}{750}$	60 min.	30 min.	4 c.c.	0

It is apparent that a dilute solution $\left(\frac{N}{1000}\right)$ of potassium cyanide when applied to the surface of the pancreas is capable of inducing a glycosuria of slight degree, which is dependent not on the transportation of this poison to some distant part by means of the blood, but on its direct influence on the cells of the gland. There is, of course, no evidence that there are not other cells in the body which react to

[1] The animals were in almost every instance fed on lean meat.

hydrocyanic acid in such a way as to provoke glycosuria; but experiments made upon the cerebral cortex, the liver, the spleen, and the decapsulated kidney gave negative results. These various experiments with potassium cyanide, in connection with the observed sensitiveness of the pancreas to local applications of adrenalin, point to the pancreas as the part chiefly concerned in the production of adrenalin glycosuria, although here, again, there is no proof that some cells other than those of the pancreas do not possess a similar sensitiveness.

How the application of adrenalin to the pancreas initiates those hepatic changes which result in glycosuria is not yet clear. We at one time thought it possible that during the glycosuria something leaves the pancreas by the pancreaticoduodenal vein which stimulates the conversion of glycogen into sugar. Experiments designed to test this idea did not give it any support. At present it appears much more likely that the glycogenetic function of the liver is stimulated through the mediation of the sympathetic nervous system. No direct investigation of this phase of the subject has yet been made.

As to the way adrenalin acts on the cells of the pancreas there is no positive information, although there are two considerations which led us to conclude that the disturbance of function is of a kind that involves impaired oxidation within the pancreatic cells. One of these is that hydrocyanic acid has the property of interfering with the capacity of cells to appropriate oxygen, as was shown conclusively by the work of Geppert. It is conceivable that hydrocyanic acid has other properties which contribute to render it poisonous, but the interference with oxidation seems to sufficiently account for its powerful toxic action. It is therefore reasonable to assume that the ability of potassium cyanide to cause glycosuria is due to interference with the appropriation of oxygen by the pancreatic cells. It is possible that this disturbance in oxidation makes itself felt in an action upon the nerve-endings in the pancreas, resulting in the hepatic overaction already mentioned in speaking of adrenalin glycosuria.

What we know about the action of hydrocyanic acid led us to inquire whether there are not other poisons that have a similar action upon cells in respect to interference with intracellular oxidations. It was found that there are many substances which lead to glycosuria when applied directly to the pancreas. Comparing these with respect to their ability to oxidize or reduce, it was found that substances which exert a reducing action are more likely to induce glycosuria than those which have an oxidizing action. It must be admitted, however, that it has been possible to experiment with only a relatively small number of oxidizing and reducing agents, and that a wider experience may not sustain the generalization that the property of inducing glycosuria belongs much more to reducing than to oxidizing substances. On the

other hand, the results obtained up to the present cannot be ignored. It is impracticable to give these results in detail here, but some facts regarding them should be mentioned. Thus it was found that substances which reduce Fehling's solution occurred in the urine after the application of the following poisons to the pancreas: sulphurous acid, sulphuretted hydrogen, carbon monoxide, benzyl alcohol, and pyrogallol. Experiments with common oxidizing agents gave results quite different from those obtained with the reducing agents just mentioned. Chlorine-water (saturated solution), bromine-water (saturated solution), potassium chlorate (10 per cent. solution), hydrogen peroxide (saturated solution, fresh), chromic acid (2 per cent. solution), and nitric acid (2 per cent. and 10 per cent. solutions) all yielded negative results when painted on the pancreas. Among the oxidizing agents tried, only nitrobenzol (4 per cent. to 10 per cent. solutions) gave sugar, but a more thorough search would doubtless reveal others which have this effect.

Among substances which have little or no reducing action, but produce glycosuria, may be mentioned sodium salicylate[1] (50 per cent. solutions) and potassium cyanide. On the other hand, sodium thiosulphate (10 per cent. to 90 per cent. solutions), a powerful reducing agent, wholly failed to induce glycosuria.

It is thus clear that we cannot attribute the experimental glycosurias that have been observed merely to the reducing properties of the substances employed, but rather to some obscure toxic action exerted probably on the cells of the pancreas.[2] What we know of the action of potassium cyanide indicates that this toxic action involves interference with intracellular oxidation.

It seemed possible at first, that experimental adrenalin glycosuria might be referable to a temporary inhibition of that function of the

[1] TABLE SHOWING EFFECT OF APPLYING SODIUM SALICYLATE SOLUTION TO PANCREAS.

Weight of dog.	How applied to pancreas.	Am'nt of soluti'n used.	Strength of solution.	Duration of application.	First catheterization after	Vol. of urine.	Sugar.	Remarks.
12.7 kilo	Painted.	1 c.c.	50 %	15 min.	2 hours.	13 c.c.	2.0 %	
7.7 "	"	2 "	"	25 "	2 "	16 "	3.8 %	
7.7 "	"	1 "	"	15 "	3 "	25 "	0.2 %	
.....	Injected.	5 "	"	.....	1 h. 50 m.	4½ "	0.3 %	
9.1 kilo.	"	2 "	"	.....	2 hours.	12 "	2.8 %	
10.4 "	Painted.	1 "	"	7 min.	1 h. 30 m.	.....	9.0 %	Application to tail of pancreas.
5.4 "	"	½ "	"	30 "	2 h. 30 m.	18 c.c.	8.5 %	Application to head of pancreas.

[2] There is no direct evidence that these substances act only on the pancreas, but the cyanide experiments suggest that this may be the case. We hope to have the opportunity to test this question individually with the different poisons that occasion glycosuria.

pancreas which normally prevents the excretion of sugar, but this view soon became untenable for the following reason: If one cuts transversely through the pancreas and duodenum, so that the severed portions of the organ have their only vascular connection through the general circulation, the application of a weak potassium cyanide solution to either portion of the gland is still liable to induce glycosuria. We know from experiments already mentioned that potassium cyanide injected into the circulation failed to cause glycosuria; hence we are justified in assuming that when the cyanide acts on one part of the divided pancreas it has no influence upon the remaining portion, but acts wholly by means of this local action. As it is well known that dogs with one-half the pancreas intact do not develop glycosuria, it is evident that we have in the phenomena of cyanide glycosuria something distinct from the glycosuria that follows extirpation of the pancreas.

When the pancreas is divided in the manner just mentioned the application of a small quantity of adrenalin chloride (1 c.c. of a 1 : 1000 solution) to either end of the gland is generally followed by glycosuria. We know that when adrenalin is injected into the circulation it is capable, unlike dilute solutions of potassium cyanide, of inducing glycosuria; hence this method of experimentation does not enable us to exclude some action of adrenalin upon the unpainted part of the gland and upon other organs, yet the cyanide experiment makes it highly improbable that such action upon the unpainted gland is necessary for the production of glycosuria.

We have at present no indication whether an application of potassium cyanide or adrenalin to the pancreas acts chiefly upon the secreting glandular cells, the cells of the islands of Langerhans, or the nerve endings in the pancreas. As the islands of Langerhans have been shown by Opie to be somewhat more numerous in the tail of the dog's pancreas than in other parts, it was thought desirable to make a series of observations in which the caudal half of the organ was painted with adrenalin, and a second series in which the cephalic and descending half of the gland was so painted. There are fifteen observations in each series. As regards the weights and feeding of the dogs and the operative conditions of the experiments, the two series of observations are comparable. The pancreas was in each case severed into two approximately equal parts, the duodenum being also cut through. The amount of adrenalin chloride solution (1 : 1000) varied from 1 c.c. to 2 c.c., according to the weight of the animal. The time required for the application of the adrenalin solution was usually fifteen or twenty minutes. The urine was collected hourly by catheter for three or four hours after the paintings. Considerable variations in the degree of glycosuria were, as usual, noticeable in different animals. The total excretion of

sugar noted in fifteen dogs of the first series, in which the tail half of the pancreas was painted, was 17.25 grammes. The total excretion of sugar by the fifteen dogs of the second series, in which the cephalic half of the gland was painted, was 15.60 grammes. It cannot, of course, be maintained that these results prove the caudal end of the pancreas to be more sensitive to the action of adrenalin than the cephalic half. To determine whether this is actually the case much more numerous observations would have to be made. On the other hand, the results of our experiments are in no way opposed to the possibility that adrenalin exerts its influence through the islands of Langerhans—a possibility which naturally suggests itself, although there is no proof that adrenalin acts exclusively on the pancreas in the production of glycosuria. Some light may perhaps be thrown on this question by a study of the histological conditions in the pancreatic glands of animals that have been treated with intraperitoneal injections of adrenalin through a long period of time.

It has not been possible to induce a permanent glycosuria by means of repeated intraperitoneal injections; but in one dog in which such injections had been made at short intervals during five weeks, with a glycosuria broken only by short intermissions, the islands of Langerhans showed no alterations.

Fatal intraperitoneal doses of adrenalin may set up an acute hemorrhagic pancreatitis in which some of the islands of Langerhans, together with other structures, suffer alteration; but control experiments with intravenous injections indicate that the lesions observed are not necessary to the production of glycosuria.

On Certain Relations between the Adrenal Glands and Carbohydrate Metabolism. The knowledge that extracts of the adrenal gland have the property of inducing glycosuria suggested the inquiry whether the adrenal glands normally possess any influence on carbohydrate metabolism by virtue of their internal secretion. Experiments showed that compression of the adrenal glands is followed by glycosuria; while their exclusion, by extirpation or ligation of their vessels, is followed by a considerable fall in the sugar-content of the blood. These results were confidently interpreted as indicating that the adrenal glands stand in an important relation to carbohydrate metabolism and normally exert a regulatory influence upon the sugar-content of the blood.[1] Unforeseen experimental difficulties have up to the present time made it impossible to prove whether the influence of the adrenals on carbohydrate metabolism is of the nature suggested in the hypothesis that was proposed—that is to say, an influence exerted through the internal secretion of the gland. It is not without interest

[1] Medical News, October 25, 1902.

to review briefly the main facts that have come to light in the course of this study.

On subjecting the adrenal glands of normal dogs (fed on lean meat) to intermittent compression between the thumb and finger glucose quickly appears in the urine. The percentage of sugar may be high (4 or 5 per cent.), but the amount has never been large, and the duration of the glycosuria is not more than a few hours. It is not necessary in order to obtain these results to compress the gland to the point where its structures yield sensibly to the fingers. Control observations on the spleen, in which the organ was much damaged by pressure, failed to show glycosuria. Destructive compression of the pancreas may be followed by the appearance of a small amount of sugar in the urine.

These results were at first interpreted to indicate that the process of compression leads to glycosuria by causing a substance allied to the glycosuria-producing substance of adrenal extracts to enter the blood. It now appears uncertain whether this is the real explanation. In animals the carotids of which were connected with a mercury manometer the adrenal glands were intermittently compressed without giving rise to any increase in the general blood pressure such as one might perhaps expect if the internal secretion of the gland were actually being forced into the circulation in unusual amount. This observation, together with the fact that compression of the pancreas may occasion glycosuria, makes it necessary to admit that nervous influences may be largely responsible for the sugar which appears after compressing the adrenals. Nevertheless, the fact that compression of a single adrenal gland may occasion pronounced glycosuria suggests that functional disturbances in this gland readily bring on at least a temporary glycosuria.

Numerous experiments have been made in which the adrenal vessels were either ligatured or in which the adrenal glands were extirpated bilaterally. In most of these observations the blood sugar-content before operation was compared with the blood sugar-content about four hours after operation. A considerable fall in the percentage of blood sugar was found in almost all instances. Controls show that this fall cannot be accounted for either by the slight lengthening of the fasting period or by the small amount of blood (8 to 25 grammes) abstracted for the determination of the blood sugar.

In a few instances the blood sugar after operation on the adrenals has been somewhat increased after the lapse of four hours. There is good reason to think that etherization usually increases somewhat the sugar-content of the blood, and it is likely that our exceptional results can be accounted for by the action of this anæsthetic. The fact that we do not know any narcotic or anæsthetic which does not in itself affect the sugar-content of the blood is still an obstacle to the correct

TABLE ILLUSTRATING THE FAILURE OF ADRENALIN TO INDUCE GLYCOSURIA.

Weight of dog.	Nature of diet, etc.	Nature of operation on adrenals.	Interval between operation and injection of adrenalin.	Dose of adrenalin.	Mode of administration.	Catheterization following adrenalin after	Volume of urine.	Sugar.	Remarks.
6.9 kilo.	Lean meat.	Adrenal vessels ligatured.	3 h. 25 min.	5 c. c. (1–1000)	Intraperitoneal	1 hour. 2 hours. 3 " 4 "	5 c. c. 4 " 8 " 13 "	Trace. Negative. Trace. Negative.	A second injection of 9 c.c. adrenalin (1–1000) on following day, quite negative as regards sugar.
6.8 kilo.	Unknown; well nourished; lacteals full.	Adrenal vessels ligatured.	4 h. 40 min.	5 c. c.	Intraperitoneal	1 hour. 2 hours. 3½ "	5 c. c. 4 " 12 "	Negative. " "	No fluid in peritoneal cavity.
9.1 kilo.	Lean meat.	Right adrenal vessels tied; left gland removed.	4 h. 15 min.	7.5 c.c.	Intraperitoneal	1 hour. 2 hours. 3½ "	10 c. c. 4 " 9 "	Negative. " "	No fluid in peritoneal cavity.
8.7 kilo.	Lean meat, starved 60 hours.	Adrenal vessels ligatured.	4 h. 35 min.	8 c. c.	Intraperitoneal	36 min.	4 c. c.	Trace.	A subsequent injection of one sheep's gland (dried) caused the appearance of 0.5–1 per cent. reducing substance in 200 c.c. urine.
15.6 kilo.	Starved 40 hours; well nourished.	Adrenal vessels ligatured.	4 h. 20 min.	8 c. c.	Intraperitoneal	1 hour. 2 hours. 4 " 17 "	5 c. c. 12 " 40 "	Negative. Trace. Slight trace. Negative.	No fluid in peritoneal cavity.
7.7 kilo.	Starved 40 hours; fairly well nourished.	Adrenals removed.	4 hours.	5 c. c.	Intraperitoneal	1 hour. 4 hours.	3 c. c. 5 "	Slight trace. " "	No fluid in peritoneal cavity.
8.2 kilo.	Unknown; well nourished.	Adrenals removed.	3 h. 50 min.	4 c. c.	Intraperitoneal	1 hour.	3 c. c.	Negative.	
15.9 kilo.	Starved 40 hours; well nourished.	Adrenals removed.	5 hours.	8 c. c.	Intraperitoneal	1 hour. 3 hours.	10 c. c. 35 "	Negative. "	

interpretation of our results. Whether the fall in blood sugar which we have noted after the above-mentioned operations on the adrenals can be attributed wholly or in part to the exclusion of the internal secretion of these glands is not yet clear.

It is a fact of considerable interest that under certain conditions the injection of adrenalin into the peritoneal cavity failed to bring on glycosuria after the adrenal vessels had been ligatured or the adrenal glands had been extirpated. This result is the more striking because of the great regularity with which intraperitoneal injections of adrenalin induce marked glycosuria in normal dogs. If the injection of adrenalin be made within two hours of the operation on the adrenal glands glycosuria usually appears, but in every instance where the injection was not given until the lapse of four hours or a longer period sugar either did not appear in the urine or appeared in mere traces. The table on page 57 makes this point clear.

The necessity for control observations is, of course, obvious, and the following experiments are of interest in this connection:

Experiment 1. Dog; weight, 7 kilos. Poorly nourished; not fed for twenty-four hours. The mesenteric vessels passing to and from a loop of jejunum six inches in length were ligated with two ligatures, and the loop itself was tied off. No ether used. Four hours after this operation 4 c.c. adrenalin chloride solution (1 : 1000) were injected into the peritoneal cavity; 8 c.c. of urine collected one hour later showed 6.2 per cent. sugar.

Experiment 2. Dog; weight, 18 kilos. Well nourished; twenty-four hours' fast. Etherized and vessels and nerves of the spleen ligatured about one and a half inches from the spleen, numerous ligatures being employed. First hour after operation 35 c.c. urine, about 0.5 per cent. sugar; second hour after operation 10 c.c. urine, about 0.3 per cent. sugar; third hour after operation 11 c.c. urine, slight reduction; fourth hour after operation 13 c.c. urine, negative or slight trace. After four hours animal received 8 c.c. adrenalin chloride solution (1 : 1000) in the peritoneal cavity. Fifty-five minutes later 49 c.c. urine, 2.8 per cent. sugar; two hours and a half later 40 c.c. urine, 6.1 per cent. sugar.

Experiment 3. Dog; weight, 11 kilos. Well nourished; not fed for twenty-four hours. Etherized and splenic vessels and nerves tied off with numerous ligatures, as in Experiment 2. First hour after operation 14 c.c. urine gave 0.44 per cent. sugar; second hour after operation 14 c.c. urine gave a slight reduction; third hour after operation 18 c.c. urine gave a slight reduction; four and a quarter hours after operation 18 c.c. urine gave a trace of reduction. After four and a quarter hours animal received 5 c.c. adrenalin in the peritoneal cavity. Fifty minutes later 23 c.c. urine gave 1.78 per cent. sugar; two and a half hours later 35 c.c. urine gave 4.9 per cent. sugar.

These and similar control experiments show that operations on the spleen or intestine do not lead to an abolition of the property of adre-

nalin to induce glycosuria when put into the peritoneal cavity. It occurs to one that the operation of ligating the adrenal vessels or extirpating the glands may be followed by a disturbance of absorption from the peritoneum; but if this be the case it is difficult to see why it should not also follow operations on the spleen. It also occurs to one that the injected adrenalin may have been mixed with blood, and thus rendered less active; but hemorrhage did not occur in any case, and the peritoneal cavity was in several instances practically free from fluid. The failure of adrenalin to cause glycosuria in our experiments seems to point to some special influence connected with the exclusion of the adrenals; but whether the real explanation lies in the elimination of the adrenal internal secretion, or in some obscure nervous disturbance, it has not been possible to determine. It is not certain that the adrenalin used in these experiments is equivalent to the internal secretion of the dog's adrenals.

In five dogs from which the pancreas was totally removed after bilateral ligation of the adrenal vessels it was observed that the urine subsequently passed either contained no sugar or only a small quantity.

In those cases where the urine contained some sugar this disappeared before the lapse of many hours. Comparing these results with those which we have obtained from numerous extirpations of the pancreas alone, there seems to be no doubt that exclusion of the adrenal glands modifies the onset of pancreatic glycosuria in the direction of greatly reducing the early excretion of sugar.[1] Even in cases where the

[1] Experiments 1, 2, and 3 illustrate the inhibition of pancreatic glycosuria after operations on the suprarenals. A similar inhibition was not observed after ligature of splenic vessels. Controls involving operations on the nervous system only have not been made.

Experiment 1. Dog; weight, 10 kilos. Bladder emptied; urine normal. Suprarenal vessels ligatured on both sides. Immediately afterward pancreas completely extirpated.

One hour 15 minutes after pancreatic extirpation, 2¼ c.c. urine contained no sugar.

Two hours 30 minutes after operation, 6 c.c. urine contained about 0.3 per cent. sugar.

Three hours 30 minutes after operation, 12 c.c. urine with 10 c.c. Fehling's solution gave slight greenish reduction.

Four hours 30 minutes after operation, 8 c.c. urine, negative for sugar.

Experiment 2. Dog; weight, 10.9 kilos. Bladder emptied; urine normal. Suprarenal vessels ligatured on both sides; 27 minutes later pancreas had been completely extirpated.

One hour after operation, 5 c.c. urine contained about 0.5 per cent. sugar.

Two hours after operation, 4 c.c. urine contained about 0.4–0.5 per cent. sugar.

Three hours after operation, 1.5 c.c. urine contained 0.3–0.4 per cent. sugar.

Four hours thirty minutes after operation, 4–5 c.c. bloody urine contained no sugar.

Experiment 3. Dog; weight, 9.1 kilos. Bladder emptied, urine normal. Suprarenal vessels ligatured on both sides. Twenty-five minutes after completion of these operations the pancreas had been completely extirpated.

One hour 45 minutes after last operation, 6 c.c. urine contained not more than 0.2 per cent. sugar.

Three hours 45 minutes after last operation, 9 c.c. urine gave very slight reduction.

Five hours 45 minutes after last operation, 10 c.c. urine, quite negative.

Ten hours after last operation, 9 c.c. urine, quite negative.

Experiment 4. Dog; weight, 9.2 kilos. Bladder emptied, urine normal, pancreas completely extirpated. One hour later 10 c.c. urine contained 7 per cent. sugar. One hour and

adrenal operation follows extirpation of the pancreas a high grade of glycosuria may be rapidly lessened; but ultimately the excretion of sugar again reaches a high level, so that the adrenal influence, whatever it may be, is a transient one. In the interpretation of these results one has to bear in mind that the glycosuria of simple pancreatic extirpation may show for a time a spontaneous falling off in the quantity of sugar excreted. It seems to us probable that a severe form of shock may be responsible for the inhibition of pancreatic glycosuria that has been observed.

Although the experimental results that have been here described point to a closer relationship between the adrenal glands and carbo-

15 minutes after pancreatic extirpation right adrenal vessels were tied; 8 minutes later left adrenal vessels were tied. Urine collected 12 minutes later contained 6.5 per cent. sugar.

One hour after ligation of adrenals, 6 c.c. urine contained 5.6 per cent. sugar.

Four hours after ligation, 20 c.c. urine contained 4.6 per cent. sugar.

Eight hours after ligation, 20 c.c. urine contained 0.6 per cent. sugar.

Soon after suppression of urine occurred.

Experiment 5. Dog; weight, 16.8 kilos. Bladder emptied, urine normal, pancreas completely extirpated. Twenty minutes later right adrenal vessels tied. Urine obtained by catheter showed slight reduction. One hour after operation on left adrenal, 5 c.c. urine contained 6 7 per cent. sugar. Ten minutes later left adrenal vessels tied.

1 hour 15 minutes	after ligation of left adrenal vessels,	13 c.c.	urine contained	4.5	p. c. sugar.
2 hours 15 minutes	" " "	17 c.c.	"	1.6	" "
3 hours 15 minutes	" " "	40 c.c.	"	0.2	" "
4 hours 15 minutes	" " "	16 c.c.	"	0.3	" "
5 hours 15 minutes	" " "	27 c.c.	"	1.25	" "
6 hours 15 minutes	" " "	13 c.c.	"	1.75	" "
7 hours 15 minutes	" " "	4.5 c.c.	"	2.25	" "
8 hours 15 minutes	" " "	8 c.c.	"	2.25	" "

Soon after this suppression set in.

Experiment 6. Dog; weight, 8.7 kilos; starved 60 hours. Bladder emptied, urine normal, pancreas completely extirpated. Urine immediately after contained no sugar. Twenty-seven minutes after extirpation adrenal vessels tied on both sides. Urine immediately after contained no sugar.

1 hour	after ligation of adrenal vessels,	6 c.c.	urine contained	0.1–0.2	per cent. sugar.
3 hours	" "	5 c.c.	"	a trace of sugar.	
4 hours	" "		"	"	"
9 hours	" "	34 c.c.	"	"	"
23 hours	" "	12 c.c.	"	2.2	per cent. sugar.
28 hours	" "	5 c.c.	"	5.0	" "
29 hours	" "	10 c.c.	"	5.5	" "
32 hours	" "	17 c.c.	"	5.0	" "

Experiment 7. Dog; weight, 7.7 kilos; not fed for 30 hours before operation. Bladder emptied, urine normal; pancreas totally extirpated at 4.05 P.M.; aseptic operation.

2 hours	after operation,	4 c.c.	urine contained	7	per cent. sugar.
5 hours	"	45 c.c.	"	8	" "
19 hours	"	140 c.c.	"	9	" "
23 hours	"	35 c.c.	"	14.3	" "

On the following day, 23 hours after the pancreatic extirpation, the adrenal vessels were ligated on both sides.

1 hour	after ligating adrenal vessels,	11 c.c.	urine contained	6.25	per cent. sugar.
2 hours	" "	13 c.c.	"	6.5	" "
3 hours	" "	13 c.c.	"	6.5	" "
7 hours	" "	26 c.c.	"	5	" "

Subsequent collections were impracticable, although the animal lived nearly 24 hours longer.

hydrate metabolism than has been previously recognized, it cannot be maintained that we have as yet succeeded in obtaining unequivocal evidence that the phenomena described are due to the excessive influence of the adrenal internal secretion or to the exclusion of this secretion from the circulation. Some of these phenomena can probably be equally well accounted for on the supposition that imperfectly understood nervous factors have been brought into play. It must, therefore, be left to further experiments, in which close attention is given to control observations on the nervous system, to determine whether the internal secretion hypothesis is tenable.

A REPORT OF TWO CASES OF MULTIPLE SCLEROSIS, WITH NECROPSY:

WITH REMARKS ON MUSCULAR ATROPHY, SECONDARY DEGENERATION, AND LOSS OF TENDON REFLEXES, WITH INCREASED MUSCULAR TONICITY, OCCURRING IN THIS DISEASE.[1]

BY WILLIAM G. SPILLER, M.D.,
ASSISTANT CLINICAL PROFESSOR OF NERVOUS DISEASES AND ASSISTANT PROFESSOR OF NEUROPATHOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

(From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation.)

MULTIPLE sclerosis seems to be a rare disease in America, and scarcely any cases with necropsy are to be found in the literature of this country. I am inclined to think that some cases are overlooked, and that the disease, while uncommon, does occur more frequently than the paucity of records gives us reasons to believe. B. Sachs remarked at the time he wrote his critical digest on multiple sclerosis, in 1898, that he had been able to find only one necropsy record of a case of this disease published in America, and that was by Seguin, and was incomplete.

Since the publication of Sachs'[2] paper a case with necropsy has been reported by Burr and McCarthy[3] (1900), and another that probably should be classed under multiple sclerosis, although published only in abstract, May, 1902, by J. R. Hunt.[4] The paper by E. W. Taylor[5] is one of the best on the subject by American writers, but the cases he reports occurred in Germany, and are a contribution to German literature.

I report two cases, with microscopic examination of the nervous tissues. The first case was in the service of Dr. F. X. Dercum, at the

[1] Read in abstract at the annual meeting of the American Neurological Association, June 1902.

[2] Sachs. Journal of Nervous and Mental Disease, 1898.

[3] Burr and McCarthy. Ibid., 1900.

[4] J. R. Hunt. Ibid., May 12, 1902, p. 288.

[5] E. W. Taylor. Deutsche Zeitschrift für Nervenheilkunde, vol. v.

Philadelphia Hospital, and is a typical example of the disease. I am indebted to Dr. Dercum for the clinical history and the pathological material. The second case was in my service at the Philadelphia Hospital, and forms a striking contrast in its clinical aspects to Dr. Dercum's case.

CASE I.—C. O., laborer, white, aged twenty-five years, was admitted to the Philadelphia Hospital, March 26, 1900. A brief history was taken at this time.

November 6, 1900. Chief complaint: stiffness and weakness of right upper and lower limbs, vertigo, and tremor.

Father died, at the age of fifty years, from gastric disease; mother died after labor; one brother died in infancy. Three sisters and four brothers are living and well.

The patient had measles when a child and typhoid fever seven years ago. He has used alcohol and tobacco to excess, but denies venereal disease.

Two years ago last winter he worked four or five hours one night in the hold of a vessel with nothing on but trousers, drawers, shoes, and stockings. Thus clad he came up on the deck, when it was bitterly cold and raining sleet and hail, and took a drink of ice-water. He remained on deck about twenty minutes, not noticing the cold, and then returned to the hold, where he worked for six hours more. In the morning he went home and to bed, still experiencing no ill effects from the exposure. That afternoon he felt stiff all over, and the stiffness remained for several days. Four days after this exposure he had to work seven hours in the hold of a ship shovelling wet coal. While shovelling he stood in the wet coal, and afterward had to sit in the wet, shivering, while waiting for more coal. The next morning he went directly from the hold to the deck, to sweep. As soon as he reached the deck he began to feel stiff, and staggered and was hardly able to walk. That night he experienced sharp pains in the thighs, more in the right thigh, and the stiffness was most marked on the right side.

This condition remained stationary for one month, when he awakened one morning with sharp pains in the right leg, with marked rigidity of that member. Soon after this he suffered from similar pains in the left leg, although not so severely.

His condition improved slightly for several months following, but there has been little change during the past year. He has occasionally had loss of sphincter control during the past year.

Present Condition (*November* 6, 1900). The patient is a well-developed young man. His intelligence is not impaired, but his speech is slow and scanning. Pupils are equal and the irides respond promptly to light and in accommodation. The ocular muscles are apparently normal. There is a slight tremor of the tongue. The tendon reflexes of the upper limbs are normal (later those of the right upper limb were exaggerated). The epigastric reflex is normal, but the abdominal and cremasteric reflexes are absent. The patellar reflex is exaggerated on each side, more so on the right side. Ankle clonus is present on each side. Babinski's reflex is present. Grip of the right hand by dynamometer is 41; of left, 45. He has apparently very little loss of power in the upper or lower limbs. Temperature sense is normal,

except in the feet, where there is delayed sensation, and in the toes and heel of the right foot, where there is reversal of temperature sense. Tactile and pain senses are unimpaired. Station is poor. He sways with his eyes open and falls when they are closed. Gait is staggering and the right foot is dragged. Some ataxia is observed in the upper limbs, especially on the right side. Intention tremor is present in the right upper limb.

The report of the examination of the eyes by Dr. G. E. de Schweinitz, November 18, 1900, is as follows: "Light reflex normal. Each disk atrophic; atrophy more marked on temporal side. No change in vessels except a slight perivasculitis. Well-marked nystagmus."

December 8, 1901. He has wasted very rapidly during the past two months, and during the past month has had almost absolute loss of power in his lower limbs, especially on the right side. The wasting is general. Breath smells sweetish, and examination of urine shows sugar in large amount.

The patient died December 9, 1901.

The microscopic examination of the brain and spinal cord, made by me, revealed numerous areas of sclerosis, especially in the cord. It is not necessary to dwell on the pathological condition, as it was like that commonly seen in multiple sclerosis. The case was clinically and pathologically a typical one of this disease. I had the opportunity to examine this patient frequently during his residence in the hospital.

The causative relation of cold and dampness to multiple sclerosis seems to be clearly shown in this case. Krafft-Ebing has insisted on this etiology of the disease, but it is seldom that the symptoms follow so closely the exposure, as in this case. The man C. O. developed the symptoms of multiple sclerosis after repeated and long exposure to cold and dampness in shovelling coal in the hold of a vessel. Residence in a damp house was believed to be the cause of the disease in the second case. It is probable that this was not the only cause in either case.

CASE II.—The patient, a woman aged fifty-one years, was in my service at the Philadelphia Hospital during the summer of 1901. She said the first symptoms of her disease began in 1891 or 1892 after a residence in a damp house. She denied venereal disease and abuse of alcohol, although she acknowledged that she had used much tobacco. Impaired gait was noticed early, but the gait soon improved, and later became worse again. She was able to walk until 1899, but staggered so that she had to be supported. In 1891, while doing housework, she suddenly became numb in the feet, and the numbness extended gradually up the limbs, with progressive loss of power. In two days the numbness had extended to the waist, and she had a girdle sensation of pressure and incontinence of urine and feces. Her speech was slow, and she had some difficulty in saying words. My notes, made June 24, 1901, are as follows:

The lower limbs appear to be completely paralyzed, and although they are drawn up at times, the movement is probably entirely involuntary. When told to move her toes she is unable to do so. The lower limbs are wasted. The right thigh in its middle portion measures

thirteen inches; the left thigh in the corresponding portion measures fourteen inches. The thighs are proportionately more atrophied than the legs below the knees, but the atrophy in the latter is partly masked by œdema. The feet are very œdematous and pit on pressure. Pressure over either leg causes the leg to be drawn up; this is especially true of the left lower limb. The movement is the result entirely of reflex action, and is involuntary. The knees and feet are inverted, and there is much spasticity of the lower limbs, which is greatly increased by passive movement. *There is no knee-jerk on either side, even with reinforcement.* This is especially noteworthy because of the spasticity in the lower limbs. The knee-jerk is not prevented by the spasticity, as the spasticity is comparatively slight when the limbs have not been irritated, and even without irritation of the limbs there is no knee-jerk. When the attempt is made to obtain the knee-jerk there is no contraction visible in the quadriceps muscle of either side. Ankle clonus is not obtained on either side. The Babinski reflex is very pronounced on each side, the great toe as well as the other toes being drawn forcibly upward. The Achilles jerk is absent on each side. Sensation for touch, pain, and temperature is normal in the lower limbs. No tenderness is produced by pressure of the nerves or muscles.

The movements in the upper limbs are free, and the resistance to passive movements in these limbs is proportional to the muscular development. The upper limbs above the elbow are fairly well developed. The interossei muscles, the thenar and hypothenar eminences are much wasted, and the grasp of each hand is almost *nil*. The forearms are wasted, but not intensely so. Sensation for touch, pain, and temperature is normal in the upper extremities and over the chest. The tendon reflexes of the upper limbs, biceps tendon, triceps tendon, and wrist-jerks on either side are not strikingly abnormal. No tenderness is felt on pressure of nerves or muscles.

The cranial nerves are not distinctly implicated. The tongue is protruded straight. The masseters contract firmly. The corner of the mouth is drawn up well on each side, and the eyes are firmly closed. At the present examination there is considerable swelling of the left eyelid.

The spinal column is normal.

The mentality is feeble. The patient replies correctly to questions, but her statements concerning her past condition are not fully reliable. She complains of numbness in her hands. She has incontinence of urine and feces.

The report of the examination of her eyes, made by Dr. H. F. Hansell, June 24, 1901, is as follows:

"Paralysis of the third nerve of the right side and also of the left, amounting to almost complete ophthalmoplegia. Pupillary response is good. Pupils are equal. Partial atrophic cupping of both optic nerves, with reduction in size of the bloodvessels, without signs of previous inflammation."

The patient grew gradually worse, and died July 5, 1901.

The microscopic examination, made by me, gives the following results:

Numerous sclerotic areas are found throughout the brain and spinal cord. One such area is found implicating the nuclei of the oculomotor, trochlear, and abducent nerves, but is not confined to these nuclei. The nerve cell-bodies of the oculomotor nuclei are not very distinctly diseased, as shown by the thionin stain, and yet some may be slightly altered. The posterior longitudinal bundle on each side is in the sclerotic area, and contains at this part a few medullated nerve fibres. Half of the medulla oblongata at one level has undergone a sclerotic change. A sclerotic area is found in the left optic nerve, but the right optic nerve appears to be normal.

Some degeneration, as shown by the Marchi method, is detected in the sclerotic areas of the spinal cord. Secondary degeneration of moderate intensity is found in each crossed pyramidal tract, below the

FIG. 1.

CASE II.—Section through the nuclei of the oculomotor nerves, showing a sclerotic patch implicating these nuclei.

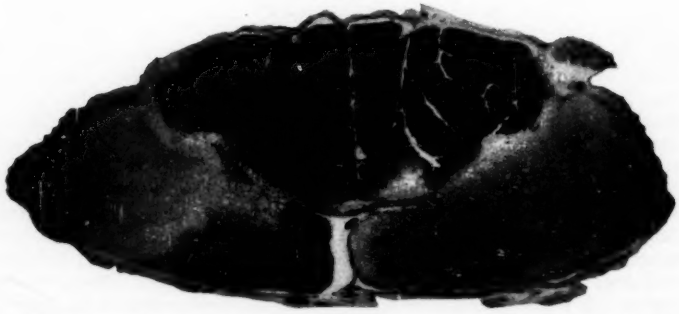
mid-thoracic region, but is greater on one side. No sclerotic areas are found in the posterior columns at the upper lumbar region, but in the mid-lumbar region a sclerotic area is present on each side of the posterior septum, and implicates the posterior root fibres after their entrance into the posterior columns. These areas do not extend into the lower lumbar region, but here a sclerotic area is found implicating one anterior horn and the antero-lateral column. A sclerotic area implicates the greater part of the left anterior and lateral columns and the gray matter of the left side and a part of the left posterior columns in the sacral region. A sclerotic area is found also in the right lateral column, and gray matter of the right side in the sacral region. Many of the nerve cell-bodies of the anterior horns of the cervical and lumbar region appear shrunken and have imperfect dendritic processes, and some are much pigmented. The thionin stain was employed. The

nerve cell-bodies in a sclerotic area implicating one anterior horn in the lower lumbar region resemble very closely those of the other horn

FIG. 2.

CASE II.—A sclerotic area implicates a large portion of the medulla oblongata.

FIG. 3.



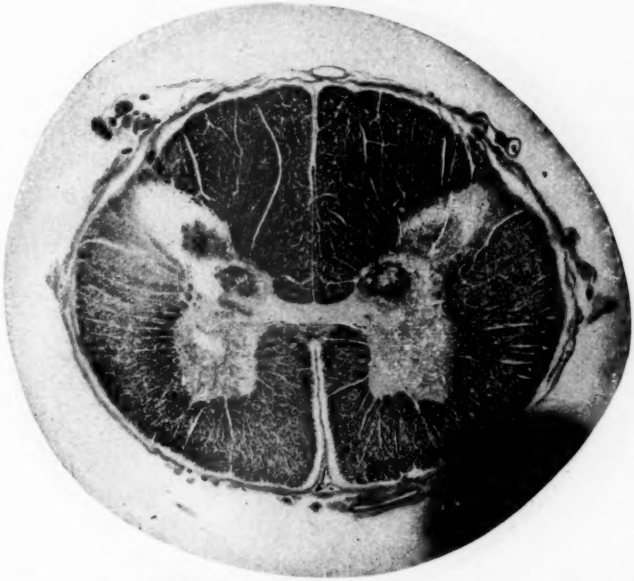
CASE II.—Section from the cervical region, showing a large sclerotic patch on each side of the spinal cord.

in the same section where there is no sclerotic area, and in neither horn are they normal. A branch of one of the plantar nerves is partially degenerated. Many other sclerotic areas not described are found in the brain and spinal cord.

A summary of the case is as follows:

In 1891 the patient—a woman, then about forty-one years of age—complained of numbness in the feet, and soon the legs became numb. She had at this time progressive loss of power in the lower limbs and

FIG. 4.

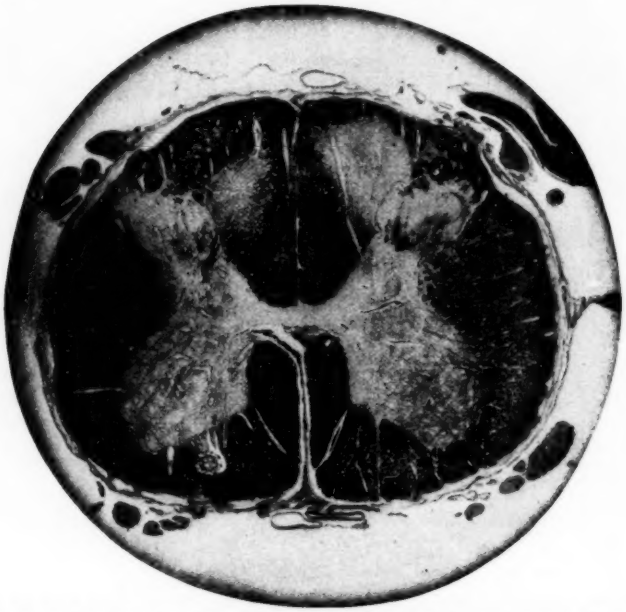


CASE II.—No sclerotic area is seen in the posterior columns in this section from the upper lumbar region. The secondary degeneration of the crossed pyramidal tracts is not well reproduced in the photographs.

staggering gait. Within two days the numbness extended as high as the waist, and she complained of girdle sensation, and had complete paralysis of the lower limbs. She had also incontinence of urine and feces. She had resided in a damp house. The disturbance of gait soon disappeared for a time, and she was able to walk with difficulty until 1899, but staggered. She complained of shooting pains at times in the knees, extending to the ankles. In 1901 her speech was somewhat drawling. The lower limbs were completely paralyzed, were much wasted, and spastic; slight irritation causing the limbs to be drawn up involuntarily, and yet the patellar and Achilles reflexes

were absent. The knees and feet were inverted. The Babinski reflex was very pronounced. Sensation was normal everywhere. Voluntary movement in the upper limbs was impaired, and the grasp of the hands was very feeble. The hands were very much atrophied. The tendon reflexes of the upper limbs were normal. Mentality was feeble. She had almost complete external ophthalmoplegia and partial atrophic cupping of both optic nerves. Iritic response was good. The case was one of disseminated sclerosis, as shown by the microscopic examination.

FIG. 5.



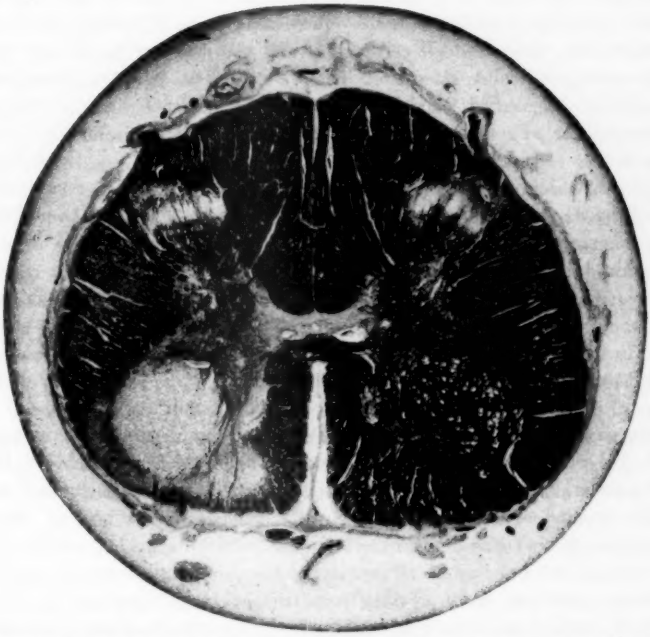
CASE II.—Section from the mid-lumbar region. A sclerotic area is seen on each side of the posterior septum only in the mid-lumbar region (compare Fig. 5 with Figs. 4 and 6). The tendency to symmetry of the areas in multiple sclerosis is well shown in this section.

The interesting features of this case were: The pronounced muscular atrophy; the secondary degeneration of the crossed, pyramidal tracts, more distinct, however, on one side, in a case of disseminated sclerosis; the loss of the patellar and Achilles reflexes, with spasticity of the lower limbs, the loss of these reflexes probably being the result of sclerotic areas in the posterior columns and a part of the anterior horns of the lumbar and sacral regions; and the almost complete external ophthalmoplegia resulting from a sclerotic area in the nuclei of the third, fourth, and sixth nerves.

The muscular atrophy was very pronounced in the lower and upper limbs, and in the latter the atrophy was more distinct in the small muscles of the hands. The atrophy in the lower limbs below the knees was partly masked by œdema. Oppenheim[1] regards muscular atrophy as a rare sign of multiple sclerosis, and states that, as a rule, the muscles preserve their normal size and electrical reactions.

L. Brauer[2] believes that muscular atrophy is very uncommon in the early stages of multiple sclerosis, and he reports a case of this disease

FIG. 6.



CASE II.—Section from the lower lumbar region. The sclerotic areas of the posterior columns represented in Fig. 5 have disappeared, but a sclerotic area is seen in one anterior horn extending into the white matter.

in which muscular atrophy was an early symptom and later became very pronounced. He acknowledges that muscular atrophy does occur occasionally in multiple sclerosis, and he believes it affects especially the small muscles of the hand and the peroneus distribution. He refers to cases of muscular atrophy occurring in multiple sclerosis reported

[1] Oppenheim. Lehrbuch der Nervenkrankheiten, third edition, p. 314.
[2] Brauer. Neurologisches Centralblatt, July 15, 1898, No. 14, p. 635.

by Jolly, Ebstein, Leube, Schüle, Buchwald, Otto, Engesser, Dejerine, and Pitres. Killion also is said to have observed muscular atrophy in multiple sclerosis.

Probst[1] speaks of the infrequency of muscular atrophy in multiple sclerosis, and refers to a few cases in which it was observed. In most of these cases no very important alteration of the cell-bodies of the anterior horns was seen, but Probst was able to find a decrease in the number and a shrinkage of the cell-bodies in the anterior horns of the upper cervical region in one case of multiple sclerosis with muscular atrophy, although no sclerotic focus could be found in this region. This case Probst pronounces as unquestionably one of multiple sclerosis. Alteration of the nerve cell-bodies was observed by me in my case. According to Probst, alteration of nerve cell-bodies in multiple sclerosis has been observed by Bourneville, Guérard, Charcot, Fromann, Gowers, Obersteiner, Frommann, Taylor, Schuster, and Bielschowsky; but muscular atrophy does not appear to have been observed in all these cases in which cellular change existed.

Secondary degeneration is not seen in multiple sclerosis, according to some writers, and yet in my case it could be found in the crossed pyramidal tracts in the spinal cord below the mid-thoracic region. According to Probst,[2] Schultze was the first to offer as an explanation of the absence of secondary degeneration the preservation of the axons in the sclerotic foci. Secondary degeneration in multiple sclerosis is said to have been observed by Jolly in 1872, Buss in 1889, Werdnig in 1888, Babinski in 1885, Redlich in 1895, and Rossolimo—certainly a small number of cases, in consideration of the large number of cases of this disease published. In most of the cases in which secondary degeneration was found it extended only a short distance, and was only of moderate degree. In a case reported by Probst[3] secondary degeneration of the anterior and lateral pyramidal tracts existed, and extended from the proximal portion of the pons into the lumbar region. Probst mentions that possibly some might regard his case as one in which multiple sclerosis was combined with amyotrophic lateral sclerosis, inasmuch as the nerve cell-bodies of the anterior horns were not normal and sclerotic foci were not found in the spinal cord. This combination, I think, might occur, as both diseases possibly are the result of faulty development of nervous tissue in the embryo.

Since my paper was read before the American Neurological Association an interesting article in which the occurrence of secondary degeneration in multiple sclerosis is considered has been published by Schupfer.[4] He says secondary degeneration in this disease has been observed only

[1] Probst. Deutsche Zeitschrift für Nervenheilkunde, 1898, vol. xii.
[2] Loc. cit. [3] Loc. cit.
[4] Schupfer. Monatsschrift für Psychiatrie und Neurologie, August, 1902, p. 109.

by Jolly, Westphal, Schultze, Greiff, Babinski, Werdnig, Buss, Rossolimo, Probst, Thomas and Long, and Taylor. He subjects these cases to a critical study, and concludes that only in the cases of Buss, Probst, and Thomas and Long was the degeneration of the pyramidal tracts in connection with lesions in the spinal cord, medulla oblongata, and pons. In Thomas and Long's case the cause of the degeneration he thinks was syphilitic endarteritis. Degeneration of the pyramidal tracts is therefore, in his opinion, extremely rare in multiple sclerosis, and may be caused by sclerotic foci or may occur independently of these. The secondary degeneration of the pyramidal tracts may be associated with diffuse sclerosis of the cerebral hemispheres with atrophy of the gyri and alteration of the cells of the central gyri, as in the cases of Schultze and Greiff. The occurrence of degeneration of the pyramidal tracts without focal lesions he finds difficult to explain. It is possible that Schupfer does not lay sufficient importance upon the short extent of some of the foci in multiple sclerosis, and important areas of sclerosis of limited extent may be overlooked. In Jolly's case and Schultze's, Schupfer says the sclerotic areas do not explain the degeneration of the pyramidal tracts, as the degeneration began at a part where sclerotic areas were not detected. It is important to bear in mind the cumulative effect of slight degeneration at different levels; this, however, Schupfer does not overlook.

The loss of the patellar reflexes, with increase in the muscular tonicity of the lower limbs, was noteworthy. There could be no mistake in regard to this, because in my notes made at the time of the clinical examination I underscored twice the statement bearing on this point. The statement reads: "The knees and feet are inverted, and there is much spasticity of the lower limbs, which is greatly increased by passive movement. *There is no knee-jerk on either side, even with reinforcement.* This is especially noteworthy because of the spasticity in the lower limbs. The knee-jerk is not prevented by the spasticity, as the spasticity is comparatively slight when the limbs have not been irritated, and even without irritation of the limbs there is no knee-jerk. When the attempt is made to obtain the knee-jerk there is no contraction visible in the quadriceps muscle of either side. Ankle clonus is not obtained on either side. . . . Achilles jerk is absent on each side."

Marie[1] has said that the tendon reflexes are never absent in multiple sclerosis.

The difference in the condition of muscular tonus and of the tendon reflexes in my case is most extraordinary. Van Gehuchten[2] has paid much attention to the relation of the muscular tonus to the tendon

[1] Marie. Leçons sur les maladies de la moelle.

[2] Van Gehuchten. Journal de Neurologie, August 20, 1897, No. 16, p. 305.

reflex. He believes there is a certain parallelism between the two; but the parallelism does not always exist, and the tendon reflexes may be exaggerated when the muscular tonus is not exaggerated, or the tendon reflexes may be preserved when muscular atony is found, or they may be absent when muscular hypertonia or contracture exists. I shall not discuss the theories he advances to explain these conditions, as they do not seem to me to be sufficiently founded on fact.

Strümpell[1] also believes that exaggeration of the tendon reflexes is often, but not always, associated with hypertonia of the muscles.

On the other hand, Parhon and Goldstein[2] do not believe that the condition of the reflexes is independent of the condition of the muscular tonus, and they assert that hypertonicity never occurs when the reflexes are lost, unless the reflexes are lost because the rigidity is so great that no movement is possible. These views are held also by some American authors. I show by this case that the patellar reflex may be lost when hypertonicity of the lower limbs is present and when this abolition of the reflex is not the result of immobility of the limbs from excessive rigidity. I have not been able to obtain Parhon and Goldstein's original paper, and must depend upon an abstract.

It is possible that in my case the patellar and Achilles reflexes were lost because sclerotic areas existed in the regions in which these reflex arcs within the spinal cord were contained. In the upper lumbar region no sclerotic focus was found, but in the mid-lumbar region a sclerotic patch was found in each posterior column implicating the fibres of the posterior roots after they had entered the cord. These sclerotic patches disappeared in the lower lumbar region, but at this level a sclerotic patch was found on one side implicating the anterior horn and anterior roots within the cord. The sclerotic areas found in the sacral cord were probably the cause of the lost Achilles jerk, and, in addition, the degeneration of one of the popliteal nerves examined may indicate that some of the terminal portions of the peripheral nerves were diseased. This alteration of the nerve fibres of the peripheral nerve was probably secondary to the alteration of the cell-bodies of the anterior horns of the spinal cord. The loss of the tendon reflexes of the lower limbs seems easily explained.

The exaggeration of the muscular tonicity may have been caused by the implication of the pyramidal tracts in the sclerotic areas above the lumbar region. If the impulses from all parts of the lower limbs had been almost entirely cut off it seems hardly probable that the muscular tonicity would have been exaggerated. A slight interference with the sensory impulses concerned in the reflexes may, however, be sufficient

[1] Strümpell. Neurologisches Centralblatt, July 1, 1899, No. 13, p. 618.

[2] Parhon and Goldstein. Roumanie médicale, 1899. Abstract in Revue Neurologique, March 15, 1902, p. 222.

to cause a loss of these reflexes, even in association with hypertonicity. Doubtless sufficient sensory impulses passed to the cord to cause exaggeration of the tonicity when the pyramidal tracts were diseased and the inhibition from the brain was removed.

In combined systemic disease the posterior and lateral columns are degenerated, and in some cases the spasticity later yields to flaccidity, apparently because after a certain time sensory impulses from the limbs to the cord are almost cut off, and therefore the paralysis becomes flaccid, even though the lateral columns may continue to degenerate. In illustration I refer to a case reported by Rheinbaldt,[1] in which rigidity of the lower limbs was prominent in the commencement of the palsy of these limbs, but when the patient came under Rheinbaldt's observation the palsy had become flaccid. Systemic degeneration of the direct and crossed pyramidal tracts, of the direct cerebellar tracts, and of the posterior columns was found. Rheinbaldt refers to a still more satisfactory case reported by Rothmann,[2] in which rigidity of the lower limbs gave place within two months to flaccidity.

Raymond and Cestan[3] have reported a very interesting case of disseminated sclerosis with paralysis in the associated movements of the eyeballs. The eyeballs were in a median position, and there was no ptosis. The irides reacted well to light and in accommodation. In each lateral movement of the eyeballs toward the right or toward the left the cornea was arrested about 7 or 8 millimetres from the external angle. Convergence, however, was very slightly affected. A sclerotic plaque was found implicating the nuclei of the third and fourth nerves. They quote Parinaud as saying that these associated paralyses are common in multiple sclerosis, but are usually incomplete. The ocular paralysis in Raymond and Cestan's case was incomplete, as it was in mine, and the lesions in the ocular nuclei in the two cases were similar. In a note of June 24, 1901, by Dr. H. F. Hansell, regarding my case, the statement is made that there was paralysis of the third nerve of each side and almost complete ophthalmoplegia. Iritic response was good. The pupils were equal. There was partial atrophic cupping of both optic nerves, with reduction in size of the bloodvessels without signs of previous inflammation. Dr. Hansell, in answer to an inquiry made by me, says: "'Almost total ophthalmoplegia' means in this case that the sixth nerves were also involved. Had external rotation been preserved my expression would have been 'double third-nerve paralysis,' and the word 'ophthalmoplegia' would not have been mentioned. Again, the total third-nerve paralysis could not have been present, since the report states that the pupils were responsive to light."

[1] Rheinbaldt. Archiv für Psychiatrie, vol. xxxv., No. 1, p. 57.
[2] Rothmann. Deutsche Zeitschrift für Nervenheilkunde, vol. vii.
[3] Raymond and Cestan. Revue Neurologique, January 15, 1902, p. 52.

The implication of the sixth nerves in my case, as in Raymond and Cestan's, suggested a paralysis of associated movement resulting from the destruction of the connection by means of the posterior longitudinal bundle between the nuclei of the oculomotor nerves and those of the abducent nerves. This form of paralysis is known by the Germans as blicklähmung. In my case at least the sixth nuclei as well as the third and fourth were implicated in the sclerotic area.

EOSINOPHILIA IN PELVIC LESIONS AND IN THE VERMIFORM APPENDIX.

By William H. Weir, M.D.,
FORMER RESIDENT GYNECOLOGIST, LAKESIDE HOSPITAL; DEMONSTRATOR IN GYNECOLOGY, WESTERN RESERVE UNIVERSITY.

(From the Pathological Laboratory of the Lakeside Hospital.)

In the routine microscopic examination of all tissues removed at operations in the gynecological service of the Lakeside Hospital, cells with eosinophilic granulations have frequently been observed in the tissues, especially in inflammatory conditions. In this laboratory their occurrence was first noted in the gynecological department in 1898, and subsequently so many instances were observed in all the departments of the laboratory that Howard and Perkins[1] were able to report a large number of cases. The present article deals with the material of the gynecological department alone.

Howard and Perkins in material from 825 consecutive operations in the different services of the hospital found eosinophiles in the tissues of 108 cases, or 13 per cent. Of these 80, or 74 per cent., were inflammatory; 24 cases were acute and 56 were chronic; 9 were tuberculous and 9 were syphilitic. In 120 consecutive autopsies eosinophiles in larger or smaller numbers were found in organs showing pathological changes in 27 instances. They occurred in the spleen, liver, stomach, intestines, kidney, heart, lung, thymus, lymph glands, and skeletal muscles.

These findings appear to warrant the conclusion that eosinophiles take an active part in many inflammatory processes, more especially appendicitis, pyosalpinx, and ovarian abscess, as well as in many cases of carcinoma showing inflammation; that they are often associated with polymorphonuclear neutrophiles and almost invariably with plasma cells; that their development from plasma cells and mononuclear leucocytes could be traced in many instances. These writers are of the opinion that the eosinophiles found in the tissues have usually

[1] Johns Hopkins Hospital Reports, vol. x.

emigrated from the vessels, but that in a certain proportion of cases they are formed in the lesion by transition from plasma cells and mononuclear leucocytes. Their article contains a careful review of the literature, of which two references are here applicable.

Przerwoski[1] noted them in 4 cases of carcinoma of the portio vaginalis, occurring in the connective tissue, in the carcinoma cell nests, and in the bloodvessels. He counted as many as five, ten, or fifteen in a single D D Zeiss field.

Feldbausch[2] found eosinophiles in uterine carcinoma and mammary cancer with acute mastitis, in metastases in lymph glands secondary to epithelioma of the vulva, in epithelioma of the bladder and of the lip, and in some sarcomata and lymphosarcomata. He gives many references, and quotes similar cases noted by Rimbach and Neusser.

As regards the technique employed, the majority of the tissues were fixed and hardened in Orth's fluid (Müller's fluid, 9 parts; 40 per cent. formaldehyde solution, 1 part), the best results being obtained after hardening in this for a week; they were then embedded in celloidin and stained with hæmatoxylin and eosin. The eosinophiles are also readily demonstrated after hardening with mercuric bichloride, formalin, Zenker's or Müller's fluids, and staining with hæmatoxylin and eosin, or with eosin followed by polychrome methylene blue or carbolic toluidin blue, or with the Biondi-Heidenhain triple stain. Tissues hardened in alcohol fail to show the eosinophiles satisfactorily. In specimens hardened in Orth's fluid and stained with methylene blue alone the granulations of the eosinophiles, although unstained, are plainly visible with the higher powers, while in alcohol hardened preparations, even after staining with eosin, they cannot be seen. Fine scrapings of the appendix mucosa, which almost invariably shows eosinophiles, were dropped into warm absolute alcohol with no better result. Parallel pieces of the same appendix were hardened in the usual reagents and stained as uniformly as possible. The eosinophiles were well shown after employing Orth's fluid, formalin, Zenker's and Müller's fluids, and mercuric bichloride, but they could not be found after using alcohol. The same results were obtained in a number of cases of thickened pyosalpinx when adjacent pieces of each were hardened in the different fluids.

Very satisfactory results were obtained with suitable tissues hardened in Orth's fluid and stained with eosin, followed by Unna's polychrome methylene blue or carbolic toluidin blue. The bacteria and nuclei are stained blue; the eosinophiles are very prominent, and are readily distinguished from the polymorphonuclear neutrophiles, whose protoplasm takes a slight pinkish tinge, and from the mast cells, whose large granu-

[1] Przerwoski. Centralbl. für Allgem. Patholog. und Path. Anatomie, 1896, vol. vii. s. 117.
[2] Feldbausch. Virchow's Archiv, 1900, clxi.

lations take the basic stain, being lilac-colored and darker than the bright-red eosinophilic granulations.

In inflammatory conditions the eosinophilic infiltration is usually most marked in suppurative cases or in the subacute stage. It occurs also in some recent acute and in chronic cases. These cells play a part in general cellular infiltrations in which polymorphonuclear neutrophiles, small round cells or lymphocytes, plasma cells, and mast cells also participate. The number of the eosinophiles varies within wide limits. Many of our cases showed them in the tissues, but in such small numbers that we have not included them in our list, while in others they were very numerous. Przerwoski[1] found as many as five, ten, or fifteen in a D D Zeiss field, but in several cases in selected areas we have counted as many as 250 in the smaller field of a 1/12 oil-immersion with an Oc. 4. They are usually polymorphonuclear, although mononuclear forms are also found. As a rule, they are spherical, but frequently are elongated and fusiform in shape, lying between the connective tissue or smooth muscle cells. Some of these fusiform cells may have but a few eosinophilic granulations and be mononuclear, the nucleus being vesicular and resembling those in the adjacent connective tissue cells. All intermediate forms between these and the polymorphonuclear spherical eosinophiles are seen, suggesting the possible formation of connective tissue cells from the eosinophiles, or *vice versa*. In such areas Howard and Perkins have traced the development of eosinophiles from smooth muscle fibres, and have shown that eosinophiles may be derived from plasma cells and large mononuclear leucocytes, and describe a progressive series of cells intermediate between these. We have observed these forms, but we have also frequently seen a similar series of cells intermediate in type between the plasma cell and the mast cell of the tissues, especially in the appendix mucosa, stained with Unna's polychrome methylene blue, carbolic toluidin blue, or either of these after eosin. The first stage is the formation of fine granulations in the plasma cell, which gradually become larger and stain more deeply until the typical mast cell of the type found in the tissues is reached. Whether or not this be an indication of the development of mast cells from plasma cells, or *vice versa*, the demonstration of an intermediate series of cells is at least of interest.

The pathological material upon which these observations are based was all obtained from the first 500 consecutive operative cases in which tissues were removed in the gynecological service of the Lakeside Hospital. In 145 of these cases infiltration with eosinophiles was found. The tissues from 261 of the 500 cases were hardened in alcohol, and

[1] Przerwoski. Loc. cit.

therefore would not have shown eosinophiles even had they been present; 248 of these 261 cases supplied endometrium alone or with portions of the cervix. There are left, then, only 104 cases in which appropriate fixing agents were employed and in which eosinophiles were absent or found only in small numbers. The majority of these were chronic inflammatory cases.

The 145 cases with eosinophilic infiltration showed the following pathological conditions, which are arranged in the order of their frequency, the numbers indicating the number of cases in which each condition was found. The total would greatly exceed the number of cases, from the fact that several different pathological conditions showing eosinophilic infiltration often occurred in the same patient.

Appendix, normal and diseased	56	Omentitis	4
Pyosalpinx	54	Tubal pregnancy	3
Salpingitis	33	Normal corpus luteum	3
Ovarian abscess	25	Sarcoma uteri	3
Perioöphoritis	17	Interstitial cervicitis	3
Corpus luteum cyst	12	Fibro-adenoma of the breast	2
Congestion of the Fallopian tube	11	Proctitis	2
Endometritis interstitialis	10	Malignant adenoma uteri	1
Carcinoma of the cervix	11	Suppurative metritis	1
Hydrosalpinx	6	Fibromyoma uteri	1
Oöphoritis	4	Syphilitic elephantiasis of the vulva	1

These conditions will now be considered more in detail.

Pyosalpinx was the most frequent inflammatory condition showing eosinophilic infiltration. In the 500 cases pyosalpinx was found 62 times, being usually bilateral; 54 of these cases showed eosinophiles in the tissues in large numbers; in 4 cases only a few of these cells were found, in 2 of which the tissues were imperfectly hardened, while a third showed marked eosinophilic infiltration in the other tissues removed; in 4 cases they were absent, the tissues in 3 of these having been hardened in alcohol.

The infectious agent in the majority of these cases, and in fact in most pelvic inflammatory conditions, was undoubtedly the gonococcus. In a number of instances typical gonococci were found on cover-slip examination of the pus and also in stained sections of the tissue; in many others, although the history was extremely suggestive, cover-slip examination and cultures of the pus proved negative, thus confirming the statement that in many cases the pus is either sterile or of slight virulence. Streptococcus pyogenes, bacillus mucosus capsulatus, staphylococcus pyogenes albus, and bacillus tuberculosus were the causal agents in some of the above cases.

In pyosalpinx the eosinophiles are most numerous in the muscularis, especially where this is considerably thickened. Here they are often seen assuming a spindle form and crowded into rows between the muscle and connective tissue cells. They are seen more sparsely in the stroma

of the folds, in the purulent exudate, and in the vessels; they are never so numerous in the folds as in the muscularis. In the vessels the leucocytes are often increased in number, but the percentage of eosinophiles is usually about normal, although on account of their more prominent appearance the proportion seems increased. Since the histological findings in most of these cases are very similar, a short description of one will suffice.

Gynecological Pathological, No. 465. Right perioöphoritis and pyosalpinx; left ovarian abscess and pyosalpinx. The left tube, 8 cm. in length, is much thickened, convoluted, and occluded. The lumen is distended with pus showing typical gonococci; the outer surface of the tube is covered with dense adhesions.

Microscopically the lumen contains a quantity of pus, gonococci being seen in some of the cells. The folds of the mucosa are numerous, showing a complex arrangement, but only a few adhesions. As a rule, they are greatly thickened and swollen, exhibiting dense cellular infiltration, with polymorphonuclear neutrophiles, lymphocytes, plasma cells, eosinophiles, and mast cells. The epithelium is almost everywhere intact, but is pale, swollen, and cuboidal, being scarcely distinguishable from the connective tissue cells of the folds. The cilia are usually missing, and numbers of leucocytes are found between the epithelial cells. On the more normal folds the epithelium is intact, almost normal, and shows cilia.

The muscularis is greatly thickened. The muscle cells are pale and swollen. There is a considerable increase of connective tissue and a diffuse cellular infiltration, especially with the eosinophiles, which frequently exceed 10 per cent. of all the cells in the field. Large numbers of polymorphonuclear neutrophiles, lymphocytes, and plasma cells, with fewer mast cells, are also found. The peritoneum is found beneath thick adhesions, where it forms atypical groups of pale, swollen cells.

Salpingitis, without pus formation, showed eosinophilic infiltration in 33 cases; 6 of these, although diagnosed as acute salpingitis, contained microscopically a small amount of purulent fluid in their lumina, and might come under the head of pyosalpinx; in all 6 the eosinophiles were found only in the mucosa and in small numbers, their favorite site, the muscularis, being almost normal in appearance. In salpingitis the eosinophiles are usually less numerous than in pyosalpinx, and occupy the wall of the tube in subacute cases. In many cases of chronic or "healed" salpingitis all acute cellular infiltration had disappeared, and hence eosinophiles were absent. The following case is instructive:

Gynecological Pathological, No. 305. Supravaginal hystero-salpingo-oöphorectomy for multiple fibromyomata uteri. Both ovaries and tubes macroscopically normal. Microscopically, in the right tube the lumen is empty; the mucosa is normal except for slight eosinophilic infiltration in some of the folds, which are numerous and show a normal arrangement. The surface epithelium is intact, the cells being columnar and ciliated. The muscularis shows very marked cellular infiltration,

almost entirely with polymorphonuclear eosinophiles, which are usually accumulated in masses in the connective tissue between the muscle bundles. In some fields of a 1/12 oil-immersion lens with Oc. 4, over 90 per cent. of all the cells seen are eosinophiles, as many as 250 being counted in one such field without change of focus, although an adjoining field often shows a total absence of them. This infiltration is entirely missing in about one-third of the muscularis encircling the mucosa, and in the other two-thirds no other pathological change is found. If it were not for the actual presence in the tissues of the leucocytes a diagnosis of congestion would have been made instead of acute salpingitis.

Congestion due to traumatism at operation was found in tubes presenting a normal appearance, but which were removed with uterine fibromyomata, ovarian cysts, or some condition not involving the tube itself. Microscopically the only change found in these cases is a congestion of the vessels, with an increased number of leucocytes within their lumina. The eosinophiles, while actually more numerous than normal, preserve the usual ratio to the other leucocytes, although, owing to their more prominent staining, the former appear increased. In all cases showing such congestion the eosinophiles were sufficiently increased to attract attention.

Hydrosalpinx was present in 23 of the 500 cases. In the majority of these the changes were slight in degree and chronic, all acute cellular infiltration having disappeared. This would readily account for the fact that in only 6 cases were eosinophiles demonstrated.

Tubal pregnancy was found 5 times. In 3 there was moderate eosinophilic infiltration; in another but few were found, the condition being very chronic; a pyosalpinx, however, upon the other side showed abundant eosinophilic infiltration. The tissues from the fifth case were hardened in alcohol, and showed no eosinophiles.

Ovarian abscess was present in 27 cases, in some of which the condition was bilateral. Eosinophiles were seen in large numbers in the abscess wall in all but 2 cases; in these the tissues had been hardened in alcohol. Although in many of these cases there was a definite gonorrhœal history, the specific organisms could rarely be demonstrated. The streptococcus pyogenes was found in 2 cases. One case only will be quoted, the others presenting very similar findings.

Gynecological Pathological, No. 394. Left perioöphoritis and salpingitis; right ovarian abscess and pyosalpinx. The right ovary—5 x 3.5 x 2 cm.—is of soft consistence, and shows a number of surface adhesions. On section, an abscess sac is found in its interior. The right tube is occluded, filled with pus, and densely adherent to the ovary; together they weigh 31 grammes. Microscopically, the medulla of the ovary is for the most part replaced by an abscess which appears to have formed in a corpus luteum. The abscess wall is abundantly supplied with small vessels, and shows dense cellular infiltration, especially with eosinophiles, but also with polymorphonuclear neutro-

philes, lymphocytes, plasma cells, and fewer mast cells. The eosinophiles are most numerous in the abscess wall about midway between the inner necrotic border and the sound tissue outside. They give a reddish tinge to the tissue when seen with the lower powers, and in selected areas with a 1/12 oil-immersion lens and a No. 4 ocular they sometimes represent 60 to 75 per cent. of all the cells, as many as 150 having been counted in one such field. These cells are also found in less numbers in the pus within the abscess cavity, in the cortex and tunica albuginea, and within the vessels.

Perioöphoritis representing either an acute exudation or chronic adhesions was found in 121 cases. The majority of these were chronic, and showed no acute cellular infiltration. Eosinophiles were found in only 17 of the acute or subacute cases, often associated with pyosalpinx.

Oöphoritis showing eosinophilic infiltration was found in only 4 cases.

Excluding ovarian abscess and perioöphoritis, cellular infiltration of the ovary itself is uncommon, the inflammatory process being held in check apparently by the dense tunica albuginea, as is shown in many cases of acute perioöphoritis, where the cellular infiltration is found only in the exudate upon the surface.

Corpora lutea of normal appearance in three cases showed a number of eosinophiles associated with the usual increase of the connective-tissue elements in the later stages of the corpus luteum.

Corpus luteum cysts frequently show a slight cellular infiltration in their walls which can scarcely be termed an oöphoritis. In 12 such cases eosinophiles formed a considerable proportion of the infiltrating cells. Some of these cases probably represented enlargements of the Graafian follicles, with loss of the membrana granulosa, as it is frequently impossible to differentiate the two conditions.

The endometrium showed eosinophiles in small numbers in 10 cases of interstitial endometritis; in interstitial inflammation of the cervix they were found 3 times. These numbers seem small, but the majority of these tissues was hardened in alcohol, since it is difficult to separate the clot from the tissue if Orth's fluid be used. At present, however, we employ formalin. Of the 500 cases, in 248 the tissues represented endometrium alone or with portions of the cervix hardened in alcohol.

Metritis. Six cases of very slight metritis did not show eosinophiles, but in 1 of suppurative metritis they were numerous. The following is an illustrative case:

Gynecological Pathological, No. 295. Uterus septus partialis; acute interstitial endometritis; suppurative metritis; left tubo-ovarian abscess; right salpingitis and oöphoritis; adherent appendix. The uterine wall upon the left side was riddled with small abscesses, the pus from which showed streptococci on cover-slips and cultures. Eosinophiles were very numerous in the abscess wall.

Carcinoma of the cervix occurred in 16 of the 500 cases. In only 1 of these was a hysterectomy performed, the remaining cases being so far advanced as to warrant merely a palliative curetting, which in some cases was repeated at a subsequent date. Eosinophiles were found in large numbers in 11 of the 16 cases; they were absent in 5, in 2 of which the tissues were hardened in alcohol. The favorite seat of the eosinophiles is along the advancing margin of the growth. One instance will be cited.

Gynecological Pathological, No. 319. Vaginal hysterectomy for carcinoma of the cervix occurring in a nullipara. Microscopically in this specimen the cell nests as well as the interstitial connective tissue show dense eosinophilic infiltration, most intense along the advancing margin, where they give the tissue a reddish color when seen with the lower powers. In some fields of a 1/12 oil-immersion lens more than 90 per cent. of the cells seen are eosinophiles.

Malignant adenoma of the body of the uterus was found in the material from two operations upon the same patient. Curetting was first done for diagnosis, and subsequently hysterectomy was performed. The disease was in a very early stage, and did not involve the muscularis; the eosinophilic infiltration was slight. The condition corresponded with the malignant adenoma described by Gebhard[1] as distinguished from adenocarcinoma.

Sarcoma Uteri. Three cases occurred, and have been reported in a recent article.[2] In all, eosinophiles were found among the sarcoma cells and in the muscularis of the uterine wall near the advancing neoplasm. They were not so numerous as in carcinoma of the cervix.

Fibromyomata uteri were represented in 25 of the 500 cases; in 1 eosinophiles were found associated with areas of hyaline degeneration of the tumor.

Chronic syphilitic inflammation of the labium minus—the so-called elephantiasis syphilitica—occurred once in our series. There was a great increase of fibrous connective tissue, marked endarteritis, and considerable cellular infiltration, in which eosinophiles occurred in moderate numbers.

Fibro-adenomata of the breast were removed in 2 cases as supplementary procedures to other operations. They were both small, and showed areas of myxomatous degeneration. No inflammatory process was found microscopically, but in Gynecological Pathological, No. 475, a typical intracanalicular fibro-adenoma; these cells were fairly numerous, usually mononuclear, and scattered throughout the stroma. The other case showed but few.

Vermiform Appendix. This was removed frequently as a secondary procedure to some other abdominal operation. In many of these cases

[1] Gebhard. Patholog. Anat. der Weibliche Sexualorgane, 1898.
[2] Weir. American Journal of Obstetrics and Diseases of Women and Children, 1901.

it showed but slight pathological change, such as light surface adhesions, concretions in the lumen, or sharp twists from shortening of the mesoappendix. Upon microscopic examination the greater number of these appeared perfectly normal. The occurrence of eosinophiles in the mucosa of the normal or diseased appendix is almost invariable, and as a number were examined the findings are included in this paper.

In the 500 cases the appendix was removed 69 times, and eosinophiles were found in considerable numbers in 56. Their absence in the remaining 13 is explained by the fact that in 11 the lumina were occluded, and the mucosa, in which the eosinophiles are found, was entirely replaced by connective tissue; the remaining 2 specimens were hardened in alcohol. Of the 56 showing eosinophiles 47 were microscopically normal, although 4 of these contained firm concretions in the lumen and another contained two grape-seeds; 5 showed inflammation in varying degree, 1 contained pus, the remainder showing periappendicitis. In 2 myxomatous degeneration of the mucosa was found, 1 of these being quite cystic. Another case showed cystic dilatation above a narrow constriction, and in the remaining case the appendix was occluded, the epithelial elements were entirely lacking, but some of the lymphoid tissue still remained and showed eosinophiles. One case will be mentioned.

Gynecological Pathological, No. 393. Left salpingo-oöphorectomy and appendectomy. The appendix, 8 cm. in length, was perfectly normal except for a sharp flexure due to a shortening of the mesoappendix. Microscopically a considerable proportion of the cells composing the stroma of the mucosa are polymorphonuclear eosinophiles. They represent fully 10 per cent. of all the cells, and in some fields with a 1/12 oil-immersion lens they reach 30 to 50 per cent. They are most numerous in the deeper layers around the bases of the tubular glands, but are absent in the lymphoid nodules. They are usually polymorphonuclear, but a few are mononuclear. They are, as a rule, spherical or oval in shape, but also flattened or irregular in outline. Owing to the whole cell being stained, their number seems even larger than it really is. Polymorphonuclear neutrophiles are very scanty in the mucosa, but many plasma cells and some mast cells are found.

Rectum. In 2 cases with dense adhesions portions of the rectal wall were torn away at operation. Microscopically these showed large numbers of eosinophiles in the mucosa, and also forming part of a diffuse cellular infiltration throughout the whole bowel wall. Mast cells are found in much smaller numbers.

Omentum. Frequently at operation small portions of the torn or adherent omentum required resection. In 7 cases it showed an inflammatory condition. Eosinophiles were found in considerable numbers in 4, in small numbers in 1. In the remaining 2, where the inflammatory condition was very slight, they were missing.

Circulatory Eosinophilia. An increased number of eosinophiles in the circulating blood is said to occur in certain pelvic lesions, 4 per cent. of all the leucocytes being considered the maximum normal number of the eosinophiles.

Cabot[1] says that in carcinoma of the uterus with a leucocytosis the eosinophiles in the blood are not always decreased (as they are in many other leucocytoses), nor are they increased except when bone metastases occur. He also states that in gonorrhœal infection and in many ovarian tumors there is frequently an eosinophilia, while in most leucocytoses there is a decrease of eosinophiles.

Ewing[2] also states that there may be an eosinophilia in gonorrhœal infection.

Ehrlich and Lazarus[3] admit a moderate eosinophilia in some malignant tumors.

Vosswinckel,[4] who made differential counts in a large number of cases of disease of the female genitalia, concluded that:

1. A circulatory eosinophilia is absent in diseases of the tube alone. In pus cases there may be an increase in the polymorphonuclear neutrophiles, but no myelocytes are found. In 30 cases of fibromyomata a circulatory eosinophilia did not occur, nor was it noted in 23 cases of endometritis. In both of these latter conditions, however, a leucocytosis may occur.

2. In all severe diseases of the ovary, with fever, except carcinoma of the ovary, there is a circulatory eosinophilia.

3. In the majority (10 out of 18) of cases of large ovarian cysts and suppuration of the ovary causing extensive degeneration there is a circulatory eosinophilia, and myelocytes are also found.

4. In carcinoma of the uterus the eosinophiles in the blood may be increased, normal, or decreased, there being no difference between mild and severe cases.

Vosswinckel also quotes the following:

Neusser found in ovarian disease that the eosinophiles were increased, and that the myelocytes, which are not found in normal blood, are also found.

Kopp in 5 out of 16 cases of pelvic disease found an undoubted circulatory eosinophilia.

Zappert found the eosinophiles in the blood increased in 2 cases of carcinoma of the uterus and in 1 case of sarcoma of the ovary; decreased in 1 carcinoma of the ovary.

[1] Cabot. Clinical Examination of the Blood.
[2] Ewing. Clinical Pathology of the Blood, 1901.
[3] Ehrlich and Lazarus' Die Anämie. Nothnagel's specielle Path. und Therapie, 1901.
[4] Ueber das Vorkommen von eosinophilian Zellen und Myelocyten in menschlichen Blute, Monats. für Geburtshülfe und Gyn., 1899.

Reinbach in 40 cases of malignant tumors found the eosinophiles in the blood lessened in only 1 case of carcinoma of the ovary and stomach.

Our own observations on this point are limited, but as far as they go we have found that more than 4 per cent. of eosinophiles in the blood in pelvic diseases is quite uncommon. In most instances the counts were made in the inflammatory conditions associated with leucocytosis, and in most of them the eosinophiles were decreased in number, confirming Cabot's statement. In 29 of the cases showing eosinophilic infiltration of the tissues 48 differential counts were made, and in only 3 cases was a circulatory eosinophilia found.

Gynecological Pathological, No. 349. Bilateral chronic hydrosalpinx and perioöphoritis. Leucocytes, 4800; eosinophiles, 5.12 per cent.

Gynecological Pathological, No. 124. Right perioöphoritis and hydrosalpinx; left perioöphoritis and pyosalpinx. The day before the operation the leucocytes were 20,000, with 4 per cent. of eosinophiles. Two days after operation the leucocytes had fallen to 12,000, with 5 per cent. of eosinophiles.

Gynecological Pathological, No. 63. Left ovarian abscess and pyosalpinx (streptococcus); right perioöphoritis and salpingitis. Leucocytes, 8666; eosinophiles, 5 per cent.

Four per cent. of eosinophiles occurred but once, in a case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 16,900; 3 per cent. of eosinophiles was found twice, in one case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 9740, and in a case of bilateral gonorrhœal pyosalpinx, with a leucocytosis of 9260.

In the remaining 23 cases 41 counts were made. In 20 counts made in 12 cases the eosinophiles were 2 per cent. or a fraction over; in 11 counts made in 11 cases the eosinophiles were 1 per cent. or a little over; in 10 counts made in 10 cases the eosinophiles were below 1 per cent. In all examinations at least 400 leucocytes were counted, and in none were myelocytes found. These counts were nearly all made immediately before operation. In some cases subsequent examinations were made on the first and second days after operation. A considerable number of differential counts were made in cases in which no eosinophilic infiltration of the tissues was found or in which operation was refused. The only one of these showing an increase of eosinophiles in the blood was an advanced carcinoma of the cervix. In this case 7.5 per cent. of eosinophiles were found.

Conclusions. 1. Eosinophiles take a prominent part in the cellular infiltration associated with inflammatory and suppurative processes of the pelvic organs.

2. In such conditions they usually occur in the largest numbers in the subacute stage and associated with connective tissue hyperplasia.

3. Eosinophilic infiltration is found in most cases of carcinoma of the cervix and in almost all cases of pyosalpinx and ovarian abscess.

4. In inflammatory conditions of the endometrium eosinophiles occur in small numbers and in but few cases.

5. Eosinophiles represent a large proportion of the cells forming the stroma of the mucosa in the normal and the diseased appendix.

6. In inflammatory conditions of the pelvic organs associated with an eosinophilic infiltration of the tissues the percentage of eosinophiles in the circulating blood is rarely increased, and usually decreased.

I am much indebted to Dr. William T. Howard, Jr., Professor of Pathology, and Dr. Hunter Robb, Professor of Gynecology, for kindly advice and permission to make use of the pathological material.

THE PATHOLOGY OF THE TISSUE CHANGES INDUCED BY THE X-RAY: PRELIMINARY REPORT.

By A. G. Ellis, B.S., M.D.,
of Philadelphia,
Assistant in Pathology, Jefferson Medical College; Director of Laboratory, Friends Asylum for the Insane, Frankford; Assistant Pathologist to the Philadelphia Hospital.

(From the Laboratories of the Jefferson Medical College Hospital.)

The therapeutic efficacy of the X-ray is apparently demonstrated by the results in hundreds of cases of epithelioma, lupus, sycosis, acne, and other lesions thus treated, though time is yet needed to establish the permanency of the cures reported. The clinical effects are much the same in all successful cases—lessening or cessation of pain, drying of discharge if present, smoothing of roughened surfaces, formation of scar tissue. In the case of tumors covered by the skin there is a gradual diminution in size, accompanied or not by softening. The result of overexposure or idiosyncrasy—the so-called X-ray burn—is a well-known, but now, fortunately, very rare complication. Some writers[1, 2] claim that a reaction, evidenced by a slight dermatitis or its equivalent, is necessary or desirable to obtain therapeutic effects from the X-ray, while others[3, 4, 5, 6] agree in the belief that this is not essential.

The nature of the tissue changes induced by the X-ray in producing its effects is not clearly understood. Many explanations are offered. Some of these are based on microscopic studies of tissue; others have a clinical foundation, while the only apparent basis of a certain number is the idle speculation of a fertile imagination. With the desire of adding to the knowledge of this question the writer has studied microscopically several tumors, both before and after a series

of exposures to the X-ray. This article embodies the results of these studies as well as a brief résumé of the theories and findings of other workers gained during a somewhat extensive, though not complete, examination of the more recent literature on the subject.

Oudin, Barthelemy, and Darier,[7] in a study of X-ray alopecia in guinea-pigs, found the prickle-cell layer and the stratum granulosum ten to fifteen times thicker than the normal, the individual cells being little altered. Not a single hair was visible, and there were only traces of follicles. Hair papillæ, regeneration buds, hair muscles, and sebaceous glands were lacking. The changes in the dermis were trivial compared to those of the epidermis, the connective tissue and elastic tissue networks being normal. The small as well as the large blood-vessels of both cutis and subcutis were normal, and no changes in the nerve fibres were observed. These writers conclude that the X-ray is an irritant of unusual strength, and seems to increase the vitality of the least differentiated skin elements. On the contrary, the differentiated elements—hair, nails, and glands—undergo retrogressive changes and atrophy. They do not know whether these changes are due to nervous influence or to obliteration of vessels or other circulatory disturbances.

Huntington[8] quotes Rudis-Jicinsky as stating that in the X-ray burn the lesion consists of an acute, subacute, or chronic necrobiosis. In a later article Rudis-Jicinsky[9] says: "The irritation of the peripheral extremities of the sensory nerves causes a paralysis of the vasomotors of the vascular area affected, spasmodic contraction of the arterioles and capillaries follows, and the proper nutrition of the cells is impaired. . . . With these changes, which are directly dependent upon disturbance of the circulation, there are changes in the parenchyma cells of the affected region. The death of tissue follows, being caused by permanent stasis in the bloodvessels." Huntington also quotes Gassman and Schenkel as finding the intima of arterioles and veins, especially the latter, appreciably thickened and the lumen correspondingly narrowed. This, it is claimed, is due to a deposit of reticular masses of delicate fibrous tissue. Similar processes were noted in the elastica and muscularis.

Lowe[10] mentions Lord Kelvin's demonstration of the fact that an iron bar, electrified and insulated, can be discharged or de-electrified by the X-ray. He is of the opinion that the dermatitis as well as the therapeutic results may depend upon some similar action on the trophic nerves of the parts exposed.

Veliaminoff[11] states that Glebovski noted an increase in fibrous tissue, with conspicuous elastica, in cases of lupus and rodent ulcer treated with the X-ray, and also that lymphoid and giant cells underwent fatty degeneration.

Codman[12] coincides with the opinion that attributes these lesions to a primary action on the trophic nerves of the bloodvessels and skin. "The delay in the appearance of the lesions after the exposure, their progressive character, and their failure to react to stimulating treatment are the strongest reasons for this view. The reports of microscopic examination of the excised tissue agree in stating that the smaller arterial branches are occluded, and the appearances are not unlike those of necrosis and inflammation due to other causes."

Pusey[13] says that carcinomatous masses are replaced by a degenerated, wavy substance without structure and staining a faint blue with hæmatoxylin. The contour of the epithelial cells is lost, and cell nuclei disappear. It is a "degenerative process of some sort, what, cannot be said."

Scholtz[14] says that the X-ray affects, first or entirely, the cell elements which undergo a slow degeneration. This is shown chiefly in the epithelial cells. The phenomena of this degeneration are manifold, the nucleus as well as the protoplasm of the cell being affected. Inflammatory phenomena appear when this degeneration reaches a certain stage. Vessel changes have probably much to do with the further progress and slow healing of ulceration.

Walker[15] has studied sections of a rodent ulcer healing under treatment by the X-ray, and describes the new growth as undergoing fibromyxomatous degeneration.

Blackmar[16] concludes that the X-ray causes a breaking down of malignant and non-malignant growths, the disintegrated material being absorbed. He considers the waste products from a rapidly disintegrating cancer exceedingly dangerous when thrown into the general system unless the patient is in vigorous health.

Morton[17] believes that the effect of the X-ray in the cure of disease is due to a primary chemical reaction affecting in turn the metabolic processes. He claims that under proper conditions of administration the X-ray builds up tissue, in proof of which he cites the case of a young woman treated for enlarged axillary glands. In six weeks the neck, shoulders, chest, and breast of that side had developed so markedly that the patient afterward desired the opposite side treated to restore symmetry.

Beck[18] states that an adenocarcinoma subjected to X-ray treatment showed beginning colloid degeneration, changes of the same nature being observed in the epithelium of the skin covering the tumor. Integumental specimens show thickening of the tunica intima of the small bloodvessels, fibrous tissue in reticular arrangement being deposited. The same observer[19] elsewhere states that he places before all the nutritive changes in the walls of bloodvessels and the results incident to such changes.

Bean[20] does not think the change is a destructive one. He believes that the cells are restored to their normal condition; and while there may be and often is atrophy connected with the process, there is no necrosis. This statement he contradicts later by saying that in the light of the theory he advances, X-ray burn (really a dermatitis) is what should be expected as the result of too prolonged stimulation, and the necrosis which sometimes follows the dermatitis is the logical outcome of intense inflammation. The theory referred to is based upon the principle of molecular or atomic vibration and its response to heat and light. Bean reasons that the atomic movements of cancer cells and epithelial cells, or of sarcoma cells and connective tissue cells, are not greatly different. If a cell has not wholly departed from its proper atomic motion, we might expect the restoration of that motion or a return to the normal. As the X-rays are probably ethereal vibrations of high frequency, they act by restoring this lost motion to the cell.

Lancashire[21] says the therapeutic effect is due to mechanical stimulation. The process partakes of the nature of an inflammation.

Loeb[22] after seven exposures of ten minutes each during eleven days (transplanted sarcoma in a rat) found mitoses in the cells. The tumor continued to grow, and pieces from it were successfully transplanted into other rats. Degenerative changes were present in the centre of the tumor, but Loeb states that these changes take place in many tumors without exposure to the X-ray. They were perhaps increased by such exposure.

Herzog[22] treated transplanted sarcomas in two rats. The skin over the tumor became necrotic in each case. In one the tumor changed to a cyst filled with a perfectly clear fluid material, and after the fifth exposure the whole tumor came away, leaving a clean surface.

Wiesner[23] claims that the X-ray can act as an irritant to the nervous system, as shown by two cases in which after long exposure of the head to the rays there followed headache, dizziness, vomiting, and diarrhœa. Vomiting and diarrhœa have also followed exposures in the region of the stomach. He concludes that negative ions coming out of the tube penetrate the skin and undergo a chemical change in the molecules or in the nerve endings; this indirectly causes a trophic disturbance. The skin changes are to be looked upon as secondary. This explains the long incubation period of X-ray "burn" and the inaction upon it of therapeutic agents.

Dr. W. M. Sweet, in a personal communication to the writer, assigns to the X-ray a marked effect upon the nerves of exposed areas. In support of this view he mentions the rapid disappearance or lessening of pain in nearly every case treated. In Case II. of this series he removed with a scalpel the projecting portion of the tumor—a mass 2.5 x 3.5 cm. in dimensions—without the aid of anæsthesia and with

absolutely no pain to the patient. He also mentions the case of a prominent neurologist who received four four-minute exposures in the effort to locate a supposed foreign body in the eye. Following these the left side of the face became thoroughly anæsthetic to pain and to touch, sensation of heat and cold not being disturbed. The hair also fell out, but later returned. The anæsthesia rapidly diminished.

Hallopeau and Gadaud[24] call attention to the sclerogenic action of the X-ray, to which property they attribute the ungual dystrophies and vascular dilatations produced thereby.

Rinehart,[25] after stating that he gets no results from X-ray treatment unless inflammatory action is induced, continues: "It then remains to be decided whether the inflammation causes the death of the cancer cells and tuberculous deposits or whether the effect is produced by the light itself. My own opinion is that it is the light. Simple inflammation has often been caused by caustics in and around these sores of lupus and epithelioma without producing the death of the process. A light sufficiently strong to produce an inflammation of the healthy cells of the part treated is of sufficient strength to destroy cells of lower vitality, as cancer cells are known to be. Whether the effect upon the skin is produced by the ultra-violet rays remains to be proven. That the low vacuum tube produces more effect upon the skin than the high vacuum tube might help to substantiate the statement that the effect is from the ultra-violet rays, as they are given off more freely from a low vacuum tube."

Freund[26] in an article read at the British Medical Association states that in lupus and epithelioma the improvement is due to cell infiltration and proliferation and to the influence of the X-ray in promoting the formation of connective tissue and cicatrices. In his opinion the X-ray possesses no bactericidal qualities.

Bondurant[27] states his belief that the effect of the X-ray on cellular metabolism is the essential element in determining its value in the cure of disease, and not its destructive action (of which X-ray burn is an example), nor any supposed germicidal power.

McCaw[28] reports the apparent cure of a primary epithelioma of the uvula and soft palate by the use of the X-ray after excision and curettement. After twenty exposures a portion of the remaining growth showed degeneration of the epithelial cells, the protoplasm of which was almost entirely replaced by colloid material. This was not shown in the specimen examined before treatment.

Hett[29] believes that destruction of neoplasms does not really occur, because necrosis, if the X-ray is properly applied, does not take place in the cell. On the contrary, the cells seem to have an increased instead of a diminished vitality, this restoring the tissues to their normal condition. This statement seems difficult to reconcile with the

following, made a few paragraphs later: "It is a well-known fact that oxygen is set free by the X-ray, and it is probably this factor that produces a change in the neoplasm and embryonic cells by producing disintegration."

Pernet[30] examined irradiated lupus vulgaris tissue from beyond the obviously diseased periphery. The area had been subjected six months previously to fourteen consecutive daily exposures of ten to fifteen minutes each. In some parts the collagen was disjuncted and to some extent disintegrated. The greater part of the elastin had been destroyed. Sweat glands showed surrounding infiltration and signs of disintegration. The hair follicles and sebaceous glands had also apparently disappeared. A large vessel in the subcutaneous stratum showed thickening of its walls. In places there was a fibrous change in the upper layers of the corium.

Leonard[31] says that the X-ray has both a stimulating and an alterative effect on normal tissues. On tissues of low vitality it has an alterative effect. There may be caused a retrograde metamorphosis, ending in fatty degeneration.

Rieder[32] has demonstrated an inhibitory and distinctly bactericidal action of the X-ray on artificial cultures, and the case reported by Shand[33] might suggest this effect on bacteria in tissue. The lesions in Shand's case were recurring superficial abscesses of eighteen months' duration, the pus containing the staphylococcus pyogenes aureus. Improvement began under X-ray treatment, a relapse occurring when treatment was discontinued. Irradiation was again begun and continued until permanent cure resulted.

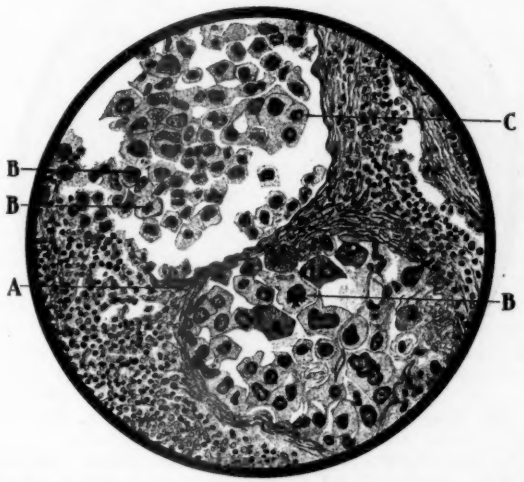
To this brief summary the writer wishes to add the following observations. For the material upon which the studies were made he is indebted to Dr. J. Chalmers Da Costa and Dr. W. M. Sweet. He also wishes to acknowledge the assistance in the study of tissue and preparation of this report rendered him by Dr. W. M. L. Coplin, who also suggested the idea and method of securing exposures of only a part of the tumor in Case I. This was accomplished by the use of a lead shield in which was made an opening corresponding in size and shape to the part to be exposed. By orienting this opening with the nipple at each application comparatively accurate placing was obtained, the exposed area being outlined with caustic at the time of the last exposure. Before the breast was removed two deep silkworm-gut sutures were passed to anchor the skin firmly to the underlying tissues, and before the removed specimen was incised the skin was further immobilized by inserting a row of sutures in the boundary of the outlined area.

In the examination of the tissues upon which this report is based the following technique was employed: Tissue, except that for study of the

nerves, was fixed in corrosive sublimate solution, hardened, and dehydrated in alcohol, and infiltrated with paraffin. Sections were stained with hæmatoxylin and eosin, hæmatoxylin and picric acid, and hæmatoxylin and Van Gieson; also with toluidin blue, Weigert's elastic tissue stain, Ehrlich's triacid mixture, and by Pianese's stain for differentiating hyalin, mucin, and colloid. Tissue for nerve study was fixed in Müller's fluid, dehydrated in alcohol, and infiltrated with celloidin, sections being stained by Weigert's method for myelin. Other pieces of the nerves were prepared by the method of Marchi.

CASE I.—M. W., aged forty-five years, patient of Dr. Da Costa. A tumor in the left breast was first noticed in July, 1901. This increased in size until February, 1902, when it was the size of a hen's

FIG. 1.



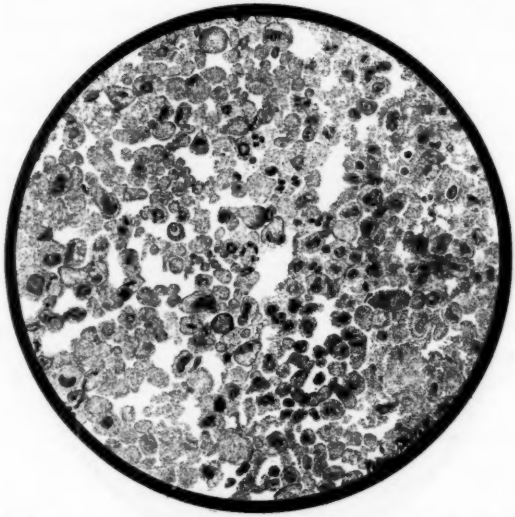
CASE I.—Scirrhous carcinoma of mamma. Section from unexposed area. A. Scanty stroma separating two alveoli. In the upper right and lower left parts of the field the extensive lymphoid and plasma-cell infiltration of the stroma is well shown. B, B, B. Cells showing atypic mitoses. C. Cells showing fusion of the protoplasm, formation of the so-called giant cells of cancer.

Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. 1/6 in. obj., 1 in. oc.

egg. Both the tumor and breast were movable, but there was axillary involvement. This proved so extensive that much of the growth could not be removed at the time of operation. It afterward grew rapidly, œdema and pain became intense, and the patient when last seen was sinking rapidly. The inner half of this tumor was given eight ten-minute exposures to the X-ray at intervals of two to three days. After the fifth treatment the exposed portion of the tumor became noticeably softer. Operation was performed March 29, 1902, by Dr. Da Costa,

the specimen received for examination being the entire breast and axillary glands. Palpation showed the exposed area to be distinctly softer than the remainder of the tumor, especially the lower end, where slight fluctuation could be detected. A needle prick into the breast just within the line separating the exposed from the unexposed areas was followed by the escape in jet of a fluid resembling serous pus. Incision of the exposed area showed surfaces studded with small, yellowish areas, apparently fatty in nature. This appearance gradually diminished toward the depth of the mass, except at the lower end, where there existed a partially filled cavity, 0.5 x 1.5 cm. in dimensions. This cavity approached closely to the skin at the point pricked

FIG. 2.



CASE I.—Scirrhous carcinoma. Section from exposed area. Field includes the contents of a large alveolus. Plasmatolysis and chromatolysis, which in parts of the section have terminated in the formation of a finely granular acidophilic detritus, are present throughout the field.

Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. 1/6 in. obj., 1 in. oc.

by the needle, and contained fluid resembling that evacuated by the puncture. The tissue surrounding this cavity showed the yellowish, fatty appearance to a marked degree. Microscopic examination of the fluid showed it to contain a moderate number of large cells, 12 to 16μ in diameter, having hyaline protoplasm and granular nuclei. Treatment with Sudan III. and osmic acid showed these cells to be practically filled with fat granules. In addition the fluid contained red and white (lymphocytes) blood corpuscles and granular débris.

Sections from the unexposed portion of the tumor (Fig. 1) show it to be a scirrhous carcinoma. In many portions of the sections are dense collections of lymphoid cells. A few polymorphonuclear leuco-

cytes and plasma cells are also seen. There are fairly numerous thick-walled bloodvessels, but very few of these show evidence of deposits on their inner surfaces. Staining by Gram's method shows the presence of a large number of small hyaline bodies resembling the so-called corpora amylacea. Mitotic cells are fairly numerous. Plimmer's bodies are present. No bacteria are demonstrable.

Sections from the exposed portion show the same general characteristics (broadly speaking), but the following differences are noted: 1. There are large areas of necrotic tissue, especially in those portions which border on the cavity described. (Fig. 2.) Some of the necrotic material is homogeneous in appearance, while other portions show the outlines of large cells, the protoplasm of which is in various stages of vacuolization and fragmentation, the nuclei having disappeared. Near the junction of these necrotic areas with the less conspicuously altered tumor are detached clusters of epithelial cells, the protoplasm of which has fused, the nuclei being in various stages of degeneration. The cells of the tumor bordering the necrotic area also show the changes just described, the degree of change becoming less as the distance from the necrosed area increases; but degenerative or necrotic changes in some degree are present in practically all the epithelial cells of this portion of the tumor, and distinct areas of beginning necrosis are scattered throughout. Special staining as well as the reactions to ordinary stains show that this degenerated material is not colloid in nature. 2. Collections of lymphoid cells are very few in number as compared with those in the unexposed portion. In the necrotic areas are a very few cells resembling polymorphonuclear leucocytes, but it is difficult to say whether they are such or are greatly changed epithelial cells with fragmented nuclei. My belief is that they are the latter. 3. Very few of the small hyaline bodies are present. 4. Some bloodvessels show endarteritis, deposits on the inner surface partially or almost wholly occluding them. 5. No mitoses are seen. Plimmer's bodies are not present in the most necrotic areas, but in other portions appear to be as numerous as in the unexposed areas. Elastic tissue is apparently more abundant than in the unexposed sections.

Case II.—W. N., aged fifty-seven years, patient of Dr. Sweet. Lymphangio-endothelioma of the orbit. The growth involved the nose and frontal sinus, and was making its appearance at the inner canthus of the opposite eye when the patient entered a distant hospital and was lost sight of. This tumor was not examined until after five ten-minute exposures to the X-ray, no tissue having been removed before treatment was begun. Sections of the tumor have for the most part a scanty fibrous tissue stroma inclosing alveoli lined with from one to several layers of large polymorphous endothelial cells. The alveoli contain masses of cells showing varying degrees of necrosis. In a few instances the outline of the cell is distinguishable, as is also the nucleus, the protoplasm being markedly vacuolated. The greater number of the cells do not show a distinct outline, the protoplasm being indistinct or irregular, or has even partially disappeared. The nuclei of these cells are fragmented, the fragments staining deeply with basic dyes. In some cells the process has gone still further, only a homogeneous material with no evidence of nuclei being present. In many of the alveoli the lining cells show the same beginning degeneration. Some of the larger necrotic areas have undoubtedly been formed

by the fusion of several alveoli, as in them fragments of degenerating trabeculæ are seen, more commonly near the periphery. Bloodvessels are fairly numerous and have very thin walls. No bacteria are demonstrable. Mast cells are present. Elastic tissue is very scanty. The necrotic changes in this tumor, though less advanced, are the counterpart of those found in Case I.

Case III.—F. M., colored, aged fifty-two years, patient of Dr. Da Costa. Ulcerated area, 9 x 12 cm. in size, of one year's duration, on inner aspect of right knee, having developed in the scar of a burn received when the patient was eight years of age. Examination of a small bit of tissue removed showed it to be a typical squamous-cell epithelioma containing an unusually large number of keratinized areas, the so-called pearls. Collections of lymphoid cells were numerous. X-ray treatment was begun and twenty ten-minute exposures of about two days' interval given. Improvement was slow, and, excessive pain persisting, the leg was amputated. Examination of the removed tumor shows only a moderate change as a result of treatment. Collections of lymphoid cells are equally numerous. Bloodvessels show an increase of fibrous tissue, with fragmented inner elastic layer. The lumen of some is occluded. Epithelial cells in areas most free from pearls show varying degrees of necrosis, as vacuolization, fusing of protoplasm, and fragmentation of nuclei. These changes can scarcely be detected in areas composed mainly of pearls, which are very numerous. Elastic tissue is very abundant, apparently an increased amount over that found in sections from the tumor before exposure. Sections stained with toluidin blue and by Gram's method show cocci and bacilli of various sizes to be exceedingly numerous. Sections of the internal popliteal nerve underlying the tumor after being treated by Marchi's method show fatty degeneration and fragmentation of some of the myelin sheaths. These changes appear to be partly of recent origin and partly of longer duration. Bloodvessels of the nerve show endarteritis, the lumen of many of them being almost obliterated.

Case IV.—R. B., aged thirty-two years, patient of Dr. Sweet. Large ulcerated surface on side of head, of ten years' duration. Growth extends posteriorly two inches behind the mastoid process and anteriorly to the orbital ridge, the ear being entirely gone. On August 7th a bit of tissue was removed for examination, which proved the growth to be a squamous epithelioma containing a few pearls. On August 14th treatment was begun. On August 29th a second piece of tissue was removed and examined, ten ten-minute exposures to the X-ray having been given. Though the clinical results were most satisfactory —cessation of profuse discharge, smoothing and healing of granulating surfaces, disappearance of pain—the microscopic changes are the least of any case examined. There is an increase of elastic tissue. In a few areas there is slight evidence of a beginning degeneration in the epithelial cells, but this is nowhere advanced. Infiltration of lymphocytes is about equal in the two specimens. Vessel walls show slight if any change. The report from this case, October 3d, is that healing still continues, but the portion of the growth from which the second specimen was removed shows the least progress. The affected area is so large that not all is exposed to the X-ray at each sitting. This probably accounts for the slight changes observed in the tissue after irradiation.

To summarize, the study of these cases shows: 1. Necrosis of cells and trabeculæ of varying degree. In Case I. there is also marked fatty degeneration. 2. Increase of elastic tissue in the three cases examined both before and after exposure. 3. Fewer areas of lymphocytic infiltration in one case after exposure, about equal numbers in the others. 4. A tendency to occlusion of vessels by deposits on their inner surfaces. This is marked in some instances, not so prominent in others. 5. Practically entire absence of infiltration by polymorphonuclear leucocytes.

Conclusions are hardly warranted by the results of these examinations, especially as further studies are being made with reference to nerve changes in irradiated tissue. Investigations regarding blood changes in persons undergoing this treatment and the tissue changes in normal rabbits that have been X-rayed are also under way. A few thoughts, however, suggest themselves:

1. Beck and others lay great stress on bloodvessel changes as the cause of necrosis. While endarteritis is probably induced by the X-ray, the accompanying tissue necrosis seems out of proportion to the vessel changes, suggesting the possibility of these being *pari passu* results of the same influence, instead of cause and effect.

2. The presence of immense numbers of cocci and bacilli in the tissues of Case III. after twenty exposures to the X-ray would argue against the possession by that agent of bactericidal power. It should be said that the pathogenicity of these organisms was not proven.

3. The unsatisfactory clinical results as well as the slight microscopic changes in Case III. can probably be safely attributed to the presence of the exceedingly numerous keratinized areas or "pearls." This emphasizes the importance of curetting or cutting away diseased tissue, whenever feasible, before instituting treatment by the X-ray.

Bibliography.

1. Rinehart. The American Journal of the Medical Sciences, July, 1902.
2. Morris and Dore. British Medical Journal, May 31, 1902.
3. Allen. Medical Record, January 25, 1902.
4. Lee. Brooklyn Medical Journal, February, 1902.
5. Brickner. Journal of the American Medical Association, May 31, 1902.
6. Leonard. American Medicine, October 4, 1902.
7. Monatshefte für Praktische Dermatologie, November 1, 1897.
8. Annals of Surgery, December, 1901.
9. New York Medical Journal, August 30, 1902.
10. British Medical Journal, January 18, 1902.
11. Russki Vratch, January 19, 1902.
12. Philadelphia Medical Journal, March 8 and 15, 1902.
13. Journal of the American Medical Association, April 12, 1902.
14. Archiv f. Dermatologie und Syphilis, Bd. lix., Heft 1, 2, 3.
15. British Medical Journal, May 10, 1902.
16. American Electro-Therapie and X-ray Era, May, 1902.
17. Medical Record, May 24, 1902.
18. New York Medical Journal, May 24, 1902.

19. Die Röntgenstrahlen im Dienste der Chirurgie, München, 1902.
20. Journal of Advanced Therapeutics, May, 1902.
21. British Medical Journal, May 31, 1902.
22. Journal of Medical Research, June, 1902.
23. Münchener Med. Wochenschr., June 24, 1902.
24. La Presse Méd., July 16, 1902.
25. The American Journal of the Medical Sciences, July, 1902.
26. Lancet, August 2, 1902.
27. New York Medical Journal, August 2, 1902.
28. Ibid., August 9, 1902.
29. Dominion Medical Monthly, August 20, 1902.
30. Lancet, September 6, 1902.
31. American Medicine, October 4, 1902.
32. Münchener Med. Wochenschr., March 11, 1902.
33. Australasian Med. Gazette, May 20, 1902.

PARACOLON INFECTIONS, WITH REPORT OF THREE CASES.

By Herbert W. Allen, M.D.,
Resident Physician, Lakeside Hospital, Cleveland.

Within the past six years, and especially within the past few months, increasing attention has been drawn to a class of cases which clinically resemble typhoid fever, but which careful bacteriological examination has shown to be due to infection by organisms intermediate between the typhoid and colon bacilli.

For these organisms and the infection which they produce the terms "paratyphoid" and "paracolon" have both been used. Achard and Bensaude,[1] who reported the first cases, entitled them "paratyphoid infections." Widal and Nobecourt[2] opposed this term, and called their organism the paracolon bacillus, claiming that it more closely resembled the colon than the typhoid bacillus. Libman[3] suggests that for the present the term "paracolon" is the preferable one, and would reserve the name "paratyphoid" for those organisms which culturally are identical with the typhoid bacillus, but which are not agglutinated by typhoidal serum.

The earlier reported cases of paracolon infection have been so thoroughly and so recently reviewed that anything more than a brief mention of them seems unnecessary at this time. Achard and Bensaude, in 1896, reported two cases. The first case resembled typhoid fever, and was complicated by double femoral phlebitis and by cystitis or pyelonephritis. From the urine was isolated a paracolon bacillus. The second case was that of an infant which developed suppuration of a sternoclavicular articulation following a febrile attack of some two weeks' duration. The joint was opened, and from the pus was grown a bacillus identical with that obtained from the first case.

In 1897 Widal and Nobecourt isolated a paracolon bacillus from an abscess in the neck, near the œsophagus.

Gwyn,[4] in 1898, reported a case which clinically was typical of typhoid fever complicated by intestinal hemorrhage. From the blood he isolated a paracolon bacillus.

Cushing,[5] in 1900, isolated a paracolon bacillus from a costochondral abscess. His patient had nine months previously suffered from an illness, with relapse, supposed to have been typhoid fever.

In 1900 Schottmüller[6] reported one case, and the following year six additional cases. In all but the last case he isolated paracolon bacilli from the blood; the serum of the seventh case agglutiuated the bacilli from certain of the other patients.

In 1901 Kurth[7] reported five cases which he considered examples of paracolon infection. From the urine of one patient and the feces of another he isolated bacilli which were agglutinated in high dilutions by the serum of four of the cases. The serum of the fifth case—the one with bacilli in the urine—was not tested.

In April of this year Brion and Kayser[8] reported a case of infection resembling typhoid, complicated by relapse and thrombosis of the left leg. A paracolon bacillus was isolated from the blood, urine, feces, vagina, and rose-spots.

In May, 1902, Strong[9] reported an autopsy done forty-two hours after death on a patient who was supposed to have died from typhoid fever. From the spleen was obtained a paracolon bacillus. No lesions were found in the intestinal tract.

In June, 1902, Buxton and Coleman[10] reported a case resembling typhoid fever from whose blood was isolated a paracolon bacillus.

In the same month Berg and Libman[11] reported an interesting case of typhoid fever with a secondary infection with a paracolon bacillus. The clinical picture was that of cholecystitis, and during life the paracolon bacillus was isolated from the gall-bladder, blood, and urine. No typhoid bacilli were cultivated, but the patient's serum agglutinated typhoid bacilli at dilutions of 1 : 250, besides giving a reaction with the paracolon bacillus. At autopsy healing ulcers were found in the ileum.

Hume[12] has recently reported a case typical of typhoid fever, with relapse, intestinal hemorrhage, and cystitis. A paracolon bacillus was isolated from the urine and feces.

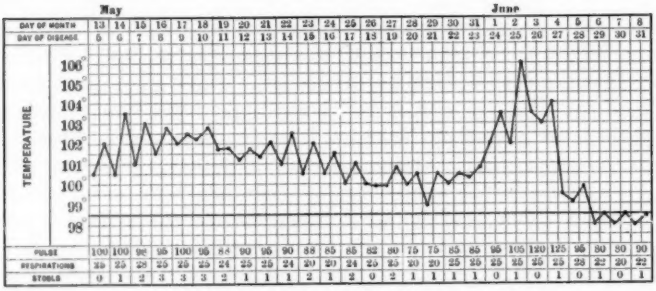
The last cases, seven in number, are reported in August of this year. Johnston[13] presents four, in two of which paracolon bacilli were isolated from the blood. In the other two the diagnosis was made on the strength of the serum reactions. There were no complications. Hewlett[14] reports one with isolation of the bacillus from the blood. His patient had a relapse complicated with bronchopneumonia. Longcope[15] reports two cases, with isolation of the bacilli from the blood in both instances. His second case had a relapse. The first case was very

severe, and proved fatal on the twelfth day of the disease. At autopsy the intestinal tract was found practically normal. This is the first complete autopsy report on a case of pure paracolon infection.

To this list I desire to add the reports of three cases recently observed at Lakeside Hospital. All occurred in the service of Dr. E. F. Cushing. The first case is to be reported later from the surgical side. Dr. G. W. Crile has kindly allowed me to use the surgical records to complete the history.

CASE I. *Paracolon infection; mild course; suppurative cholecystitis during convalescence; incision and drainage of gall-bladder; paracolon bacilli in pus; right lobar pneumonia; recovery.*—M. S., white, male, aged thirty years. Admitted May 13, 1902, complaining of headache, vomiting, loss of appetite, and general weakness. Family and past history unimportant. The present illness began four days before admission, though for two weeks past he had felt weak and drowsy, and had lost his appetite. The initial symptoms were headache, general soreness, slight cough without expectoration, and persistent vomiting. For the past four days he had vomited practically everything taken. Took to bed May 10th.

CHART I.



On examination the patient was well nourished; slightly anæmic. The tongue was dry, coated, and tremulous. Pulse slightly dicrotic. Heart and lungs negative. Liver dulness in the mammillary line extended from the fifth rib to a point two fingers' breadth below the costal margin, where the edge was distinctly felt. The abdomen was full, tympanitic, not tender. The spleen was readily palpated. There were no visible rose-spots. Temperature, 100.5° F.; pulse, 105; respirations, 25. The urine was high colored, acid, specific gravity 1025; no sugar; trace of albumin; an occasional hyaline cast and a few leucocytes. No diazo reaction.

May 14th. Widal reaction negative. No tubercle bacilli in the sputum.

From admission until May 30th the course of the disease was mild and uneventful. The highest temperature was 103.8° F.; it fell slowly and touched normal for the first time on May 29th. On May 18th the patient's serum was tested with a paracolon bacillus, but the result

was negative. On May 25th the Widal reaction was again negative. No rose-spots were ever found. The leucocyte count continued normal. In spite of the negative Widal reaction the case was considered to be a mild typhoid.

29*th*. In the evening the patient had an attack of slight abdominal pain associated with nausea and vomiting. Examination of the abdomen was negative, and the pain soon subsided.

30*th*. In the afternoon the patient again complained of abdominal pain, which he described as cramp-like and felt rather generally over the upper right half of the abdomen. The muscles over the right half of the abdomen were held slightly more rigid than over the left, and there was little tenderness on deep pressure in the right half of the umbilical region. Temperature, 100° F.; pulse, 88; respirations, 25. Leucocytes, 12,000.

31*st*. Still slight abdominal pain; nothing additional made out on examination. Lungs and heart negative. Temperature, pulse, and respirations practically unchanged. Leucocytes, 12,000.

June 1*st*. Abdominal pain still complained of, and is now located in the right hypochondrium. There is increased muscular resistance over the right half of the abdomen and decided tenderness in the region of the gall-bladder, which can now be felt as a rounded mass extending to a point 4½ cm. below the costal margin. Temperature at 8 A.M., 102° F.; pulse, 90; respirations, 25. At 8 P.M. temperature, 103.2° F.; pulse, 100; respirations, 28. Leucocytes, 10,000. No bile in the urine; no jaundice.

2*d*. The patient had a comfortable night, and this morning feels much better; abdominal pain almost gone. Examination of the abdomen shows less muscle rigidity and decidedly less tenderness, but the gall-bladder is still palpable and quite sensitive. No jaundice; no bile in the urine. Temperature, 102° F.; pulse, 100; respirations, 25. Leucocytes, 13,000. The question of operation was discussed, but it was decided to await further developments. No change was noticed until 2 P.M., when there was a return of the abdominal pain, and the patient vomited. This was repeated at 3 P.M. At 4 P.M. the patient had a hard, shaking chill, lasting ten minutes, and the temperature rose to 106° F. Aside from increased tenderness over the gall-bladder the abdominal examination remained the same. Leucocytes, 15,800.

Immediate operation was decided upon, and was performed by Dr. G. W. Crile. Cocaine anæsthesia was used. The gall-bladder was found distended and adherent to the parietal peritoneum. On incising it there escaped several ounces of a turbid fluid, which was followed by a small amount of pus. No calculi were found. The gall-bladder was drained and the wound closed. Cultures from the fluid yielded a pure growth of an actively motile bacillus with the characteristics to be described later.

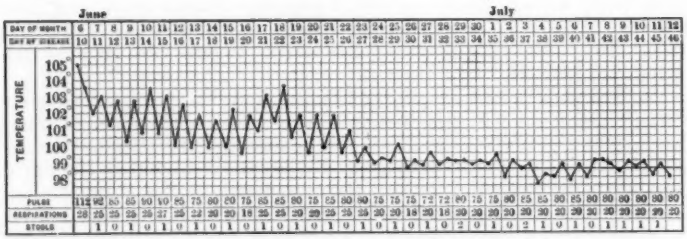
The following day, June 3d, the temperature continued elevated, and the patient complained of cough and expectoration. Examination of the lungs showed a consolidation of the lower right lobe. The next day, June 4th, the temperature fell by crisis, and thereafter continued normal throughout the patient's stay in the hospital. The lung signs cleared up rapidly.

The patient convalesced uninterruptedly, and was discharged July 6th, a very small fistula still remaining at the site of the operation.

CASE II. *Paracolon infection; mild course; cystitis on seventeenth day; thrombosis of left femoral vein on twenty-first day; paracolon bacilli from blood and urine; recovery.*—M. E., male, Australian, aged twenty-six years. Admitted June 6, 1902, complaining of headache, fever, and loss of appetite. Family and past history are unimportant. Present illness began about two weeks ago, with headache, slight cough, and coryza. For a few days had mild diarrhœa; since then has been constipated. Appetite gradually failed, and there has been rapid loss of strength. No nausea or vomiting; no chilliness; no epistaxis. Took to bed the day before admission.

Physical examination showed a well-nourished man looking decidedly ill. Expression dull; face flushed; tongue moist, coated, and tremulous. Pulse of good volume; slightly dicrotic. Lungs negative. Systolic murmur at the apex of the heart; normal area of dulness. Abdomen soft, not tender. Spleen readily palpable. No rose-spots. Liver dulness extended 4 cm. below the costal margin in the mammillary line; edge palpable. Some reddening, swelling, and tenderness about the left ankle-joint, due to a recent injury. Temperature, 105° F.; pulse, 112; respirations, 28. The urine was clear, acid,

CHART II.



specific gravity 1019; no sugar; very faint trace of albumin; no diazo reaction; microscopically contained a few coarsely granular casts.

After admission until June 16th the course of the disease was fairly typical of mild typhoid fever. The temperature was slightly irregular, ranging from 100° to 104° F. The pulse was slow, averaging 85 per minute. A few rose-spots were noted, and the spleen was always readily palpable. The leucocytes ranged from 6000 to 9000. The bowels were constipated, requiring enemata. For the first three days it was necessary to catheterize the patient; subsequently he voided urine without difficulty. The Widal reaction, tested frequently, was never positive at dilutions greater than 1 to 10. A blood culture taken June 7th yielded an actively motile bacillus, which will be described below.

On June 16th the patient first noticed slight pain in the left groin, but made no complaint until two days later. Examination at that time disclosed slight swelling of the whole left leg. The foot appeared congested, and there was marked prominence of the superficial veins of the calf and thigh. The surface temperature was not altered. On palpation there was tenderness along the course of the femoral vein and in the popliteal space. The temperature was 103.5° F., which was

about 2° higher than it had been running. The leucocyte count was 9000.

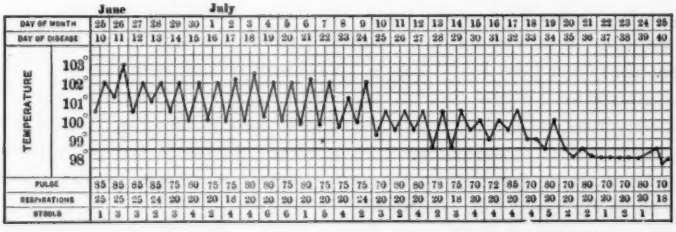
Two days later, on June 20th, a definite cord-like thickening could be made out in the upper part of the thigh over the situation of the femoral vein. This was decidedly tender on palpation. Nothing was to be felt in the popliteal space.

On June 13th pus cells were noted in the urine, and on June 21st a culture yielded a large number of colonies of a bacillus identical with that isolated from the blood; also a few colonies of a streptococcus.

The subsequent course of the disease was uneventful. The temperature reached normal on June 29th, and there was no subsequent rise. The tenderness in the left leg persisted for a few days. The leg never regained its natural size, and the superficial veins remained prominent. Under treatment with urotropin the urine cleared rapidly, and at the time of discharge contained very few pus cells, and no paracolon bacilli could be found on culture. The patient was discharged on July 12th.

CASE III. *Paracolon infection; mild course without complications; recovery.*—D. L., male, white, aged thirty-five years. Admitted June 25, 1902, complaining of fever, loss of appetite, and diarrhœa. Family

CHART III.



and past history are unimportant. For the past four weeks patient has not done any work on account of weakness and loss of appetite. On June 16th had a shaking chill, followed by fever and headache. No subsequent chills; no epistaxis. The bowels have been loose for a week previous to admission. The patient has remaind in bed since June 16th.

Physical examination disclosed a fairly well-nourished man; slightly anæmic. Tongue moist, coated, and fissured. Pulse regular, and not dicrotic. Heart and lungs negative. Abdomen held rather rigidly; no tenderness. Border of spleen palpable; a few scattered rose-spots; normal hepatic dulness. Temperature, 100.5° F.; pulse, 90; respirations, 25. Urine clear, acid, specific gravity 1015; no sugar or albumin; microscopically a few leucocytes and an occasional hyaline cast. Diazo reaction positive. Leucocytes, 4400. The Widal reaction, tested on June 29th, July 2d, 11th, and 26th, was persistently negative at dilutions of 1 : 50, though a positive reaction was sometimes obtained at 1 : 10. On July 2d and 11th the patient's serum

gave a positive reaction with the organisms obtained from the first two cases at a dilution of 1 : 50.

The course of the disease was that of a mild typhoid fever without complications. The temperature never rose above 103.5° F. It reached normal July 19th. The bowels were loose throughout the early stage of the illness. Convalescence was rapid and uneventful, and the patient was discharged July 26th. A blood culture on June 29th, the fourteenth day of disease, remained sterile. A urine culture taken during convalescence was negative for paracolon bacilli.

Bacteriology. The organisms obtained from the first two cases were practically identical, and one description will answer for both. They were very actively motile organisms, having the morphology and staining properties of B. typhosus. The growth on agar and in gelatin was similar to that of B. typhosus. Bouillon was diffusely clouded; no surface pellicle was formed after ten days' incubation. A slight trace of indol was formed in Dunham's peptone medium after one week.

On potato there was a barely perceptible growth appearing as an increase of the moisture along the line of stroke. Litmus milk was slightly acidified after twelve hours; after one week there was distinct reduction of the acidity, and by ten days the color equalled that of the control. After two weeks there was distinct alkali production. The organism from Case I. ("Samuels") produced slightly more alkali that that from Case II. ("Euster"). There was no coagulation of the milk after four weeks' incubation. Both organisms fermented glucose and maltose, with the production of acid and visible gas, but did not ferment lactose or saccharose. No animal experiments were performed. The organisms agree, therefore, very closely with most of the paracolon bacilli heretofore described.

Agglutination Tests. In all the tests a time limit of one hour was used, and a reaction was not called positive unless there was good clumping and cessation of all motility. In none of the cases was a positive Widal reaction obtained in dilutions greater than 1 : 10, though tests were made frequently throughout the course of the disease. The serum from Samuels, Case I., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 100; likewise the serum from Euster, Case II., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 200. The serum from Lawton, Case III., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 50. In addition, the sera of Cases I. and II. were tested with Gwyn's paracolon bacillus and one of Johnston's organisms, and in both instances gave positive reactions in dilutions of 1 : 50. B. "Samuels" and B. "Euster" were tested with several different typhoid sera of high agglutinative strength, but without any reaction in dilutions of 1 : 10.

The following table may assist in making these reactions clear:

Serum.	Organism.	1-10	1-50	1-100	1-200
Samuels. Case I.	Samuels	+	+	+	—
	Euster	+	+	+	—
	Gwyn	+	+	0	0
	Johnston	+	+	0	0
	B. typhosus	+	—	—	0
Euster. Case II.	Samuels	+	+	+	+
	Euster	+	+	+	+
	Gwyn	+	+	?	0
	Johnston	+	+	+	0
	B. typhosus	+	—	—	—
Lawton. Case III.	Samuels	+	+	0	0
	Euster	+	+	0	0
	B. typhus	+	—	0	0
Typhoid, agglutinative strength 1-200	Samuels	—	—	0	0
	Euster	—	—	0	0

0 = no test made. ? = doubtful reaction.

Johnston in his recent article has analyzed all the reported instances of paracolon infection. Most of the cases have run a course fairly typical of comparatively mild typhoid fever, and without the aid of the serum reaction or a bacteriological examination a differential diagnosis would be impossible. Rose-spots and a palpable spleen have been present in a majority of instances. Relapse has been comparatively common—at least five cases. Both of Longcope's cases are unusual in that labial herpes was present. The onset of one of his cases was with a chill. Our third case gave a similar history. The very wide distribution of the bacilli in the body is indicated by Brion and Kayser's case.

Many of the common and several of the uncommon complications of typhoid fever have occurred. Of the former there have been reported intestinal hemorrhage, cystitis, femoral phlebitis, furunculosis, and bronchopneumonia; of the latter suppurative arthritis, myositis, osteomyelitis, and suppurative cholecystitis.

Our first case is especially interesting as being the first recorded instance of suppurative cholecystitis complicating a paracolon infection. The clinical picture of Libman's case resembled cholecystitis, but at operation the gall-bladder was distended with dark, thick bile, and at autopsy the bladder wall showed no change. Cholecystitis, both suppurative and non-suppurative, is of course a well-recognized complication of typhoid fever, and its occurrence in a paracolon infection serves to again emphasize the marked similarity of the clinical picture of the two diseases. The ease of performance and the success of early operation in this complication is also well shown in this case.

Longcope in his paper discusses the pathology of the disease. There have been three fatal cases, with autopsies in each instance. Berg

and Libman's case was a mixed infection, probably primarily typhoid fever, with a secondary infection with the paracolon bacillus. Healing ulcers were found in the ileum. In Strong's case no clinical history is available. The autopsy was done forty-two hours after death, and Strong himself suggests that the bacillus isolated from the spleen may possibly have been a post-mortem invader. The large and small intestines were normal throughout. The mesenteric lymph glands were enlarged, and a few were hemorrhagic. Fresh smears from the spleen showed a few crescentic æstivo-autumnal malarial parasites and some pigment; but it seems unlikely that the patient's death was due to malaria. He had been treated with quinine.

Longcope's case is complete. Autopsy revealed only the lesions of an acute infection—acute splenic tumor, cloudy swelling of the liver and kidneys, focal necroses in the liver. The mesenteric lymph glands were not swollen, and both large and small intestine were practically normal.

While no very definite conclusion can be drawn as yet regarding the pathology of the disease, it is evident that we are dealing with an infection quite distinct from typhoid fever. That all of the cases of apparently pure paracolon infection may not, however, be as simple as Longcope's case might lead us to suppose is suggested by the occurrence in two instances of well-marked intestinal hemorrhages.

References.

1. Achard and Bensaude. Bull. et Mém. de la Soc. de Méd. des Hôp., November 27, 1896, p. 820.
2. Widal and Nobecourt. Semaine Médicale, August, 1897, p. 285.
3. Libman. Journal of Medical Research, June, 1902, vol. viii. No. 1.
4. Gwyn. Johns Hopkins Hospital Bulletin, 1898, vol. ix. p. 54.
5. Cushing. Ibid., 1900, vol. xi. p. 156.
6. Schottmüller. Deut. Med. Wochenschr., 1900, vol. xxvi. p. 511; Zeitschr. f. Hygiene, 1901, vol. xxxvi. p. 368.
7. Kurth. Deut. Med. Wochenschr., 1901, vol. xxvii. p. 501.
8. Brion and Kayser. Munch. Med. Wochenschr., April 15, 1902, p. 611.
9. Strong. Johns Hopkins Hospital Bulletin, May, 1902, p. 107.
10. Buxton and Coleman. The American Journal of the Medical Sciences, June, 1902, p. 976.
11. Berg and Libman. Journal of the American Medical Association, June 7, 1902, p. 1498.
12. Hume. Report of Thompson Yates Laboratories, 1902, vol. iv. p. 385.
13. Johnston. The American Journal of the Medical Sciences, August, 1902, vol. cxxiv. p. 187.
14. Hewlett. Ibid., p. 200.
15. Longcope. Ibid., p. 209.

MALTA FEVER: ITS OCCURRENCE IN THE UNITED STATES ARMY, WITH A REVIEW OF THE LITERATURE.[1]

By Charles F. Craig, M.D.,
CONTRACT SURGEON, U. S. ARMY; PATHOLOGIST AND BACTERIOLOGIST TO THE U. S. ARMY GENERAL HOSPITAL, PRESIDIO OF SAN FRANCISCO, CAL.

Historical. Medical officers of the English army were the first to draw attention to a disease prevailing in Malta and other Mediterranean stations possessing many of the symptoms of typhoid, but differing from that disease in important respects.

In 1816 Burnett[2] described very fully this disease, but regarded it as being a remittent malarial fever. This view of the character of the fever was adhered to for many years, and it was not until 1878 that the distinction was clearly drawn by medical officers of England between remittent malarial fever and Malta fever.

When first described the disease was supposed to be peculiar to the Island of Malta, hence the name "Malta fever;" but continued observation has proven that it is a widespread disease throughout tropical and subtropical regions. Thus Donaldson[3] has described cases in Gibraltar, Tomaselli in Sicily, Patterson in Constantinople, Oliver[4] along the banks of the Danube, Veale[5] in Cyprus, Musser[6] and Cox[7] in Porto Rico, and Chamberlain,[8] Curry,[9] and Strong[10] in the Philippines.

Many and various were the opinions held by observers as to the etiological factors in the production of Malta fever, and it was not until the painstaking researches of Bruce were published in 1887 that anything positive was known as to the etiology. Bruce[11] demonstrated the cause of the disease to be a micrococcus, to which he gave the name "micrococcus melitensis." His researches threw a flood of light upon the etiology and pathology of this hitherto obscure disease.

I shall not enter here into any detailed description of the pathology or symptomatology of Malta fever, save to say that it is generally a fever of long duration, subject to frequent relapses, presenting a most irregu-

[1] With permission of the Surgeon-General, U. S. A., from report to the Surgeon-General.
[2] Burnett. Practical Account of the Mediterranean Fever, London, 1816.
[3] Donaldson. Army Statistical Reports, 1839.
[4] Oliver on Danubian Fever. Lancet, 1892, vol. ii. p. 1359.
[5] Veale. Report on Cases of Fever from Cyprus, Malta, and Gibraltar. Army Medical Department Reports, England, 1879.
[6] Musser. Philadelphia Medical Journal, December, 1898.
[7] Cox. Report of Surgeon-General, U. S. A., 1899, p. 285.
[8] Chamberlain. Report of Surgeon-General, U. S. A., 1900, p. 226.
[9] Curry. Report of Surgeon-General, U. S. A., 1900, p. 226; also Journal of Medical Research, July, 1901, vol. vi. No. 1, pp. 241-248.
[10] Strong's Report of the Surgeon-General, U. S. A., 1900, p. 227.
[11] Note on Discussion of Micro-organism in Malta Fever, Practitioner, vol. xxxiv. p. 161; also Observations on Malta Fever, British Medical Journal, May 18, 1889.

lar and confusing temperature course and accompanied by severe pain in the joints, constipation, profuse perspiration, and often followed by arthritic pains, with or without swelling of the joints. An enlarged and tender spleen is very common. The diagnosis of the disease has heretofore presented many difficulties, as it resembles in many instances typhoid or remittent malarial fever; and even with the help of the microscopic examination of the blood and the Widal test the distinction between these diseases cannot always be made. In 1897, however, Wright, of the Royal Army Medical School, England, discovered that the blood serum of a patient suffering from Malta fever will agglutinate the micrococcus melitensis in very dilute solution, and that this agglutination test is most delicate and can be depended upon absolutely in diagnosis. I will give in detail the methods of performing the test later.

Description of Cases. At the United States Army General Hospital, Presidio of San Francisco, Cal., the blood of every patient admitted is examined microscopically, by order of Colonel Girard, the commanding officer. Unless specially requested by the attending surgeon, the Widal test and the agglutination test for Malta fever are not performed, so that it is possible, and indeed probable, that cases of Malta fever may have passed through the hospital without being discovered. By the courtesy of Professor Welch, Johns Hopkins University, and Professor Ophüls, Cooper Medical College, San Francisco, I have been supplied with cultures of the micrococcus melitensis, and these have been used in making the agglutination tests in the cases about to be reported.

From December 1, 1901, to date (March 24, 1902) four cases of Malta fever have come under my observation at this hospital—two during acute exacerbations of the disease and two during the chronic stage.

Case I. *Two attacks of Malta fever, the first complicated by combined æstivo-autumnal and tertian malaria.*—This case occurred in the person of an assistant in my laboratory, who had suffered repeatedly from attacks of malarial fever, and was under the medical care of Dr. Edmund Barry, to whom I am indebted for the clinical data.

History of the Case before Admission. Name, Gustav T. W. S., private, Hospital Corps; aged twenty-eight years; birthplace, Germany. Enlisted in the United States army April 7, 1898, in New York city. He arrived in New York city from Europe in 1891, and had never been sick prior to enlistment. After enlistment he was immediately ordered to Tybee Island, Ga., where he joined Battery "F," Fifth United States Artillery. He left Tybee Island with the Battery, April 23, 1898, and was next stationed at Chickamauga Park, Tenn., where he remained one week, at the end of which time he went to Fort Tampa, Fla., and about July 1st arrived at Santiago de Cuba. He had not been sick up to this time. After the surrender of Santiago he camped until about August 15, 1898, near El Caney, and while in this camp often had slight chills, followed by a rise of temperature, and was treated with quinine. Before embarking for the United States he was stationed

for one week in the city of Santiago, doing guard duty in the streets, where he had too sleep. He left, August 23d, for the United States, and went on sick report the next day, the physician diagnosing the fever from which he was then suffering as typhoid. On September 1st he arrived at Montauk Point, Long Island, where he stayed for five days, when he was transferred to St. Catherine's Hospital, Brooklyn, N. Y. Here he improved rapidly, and about September 16, 1898, was taken as a convalescent to Shepley Hall, Atlantic Highlands, N. J., through the kindness of Miss Helen Gould. About October 4, 1898, he was granted a furlough for one month to visit Brooklyn, N. Y. The next day he was seized with a severe chill, followed by high temperature, and sent by ambulance to the Methodist Episcopal Hospital, Brooklyn, where he stayed for two weeks, after which he was transferred to St. Catherine's Hospital. At this hospital his case was diagnosed as "typhoid malaria." About December 4, 1898, he reported for duty with his Battery at Fort Hamilton, N. Y., where he stayed until March 31, 1899. During this time he had several attacks of malaria, having chills followed by fever, nausea, and vomiting, pains in all the bones, and severe headache. On April 1, 1899, he left for Manila, by way of San Francisco, and was well until July of that year, when he had slight chills at San Pedro, Macati, P. I. He also suffered from attacks during August, 1899. During January, 1890, at Bacour, P. I., he had fever and chills, with severe pains repeatedly in all the joints. He was then transferred to Manila, and while on duty at the Medical Supply Depot in that city he had several attacks of fever, with pain in all the joints, severe headache, and high temperature. In November, 1900, he was ordered to the United States, his case being diagnosed as malarial cachexia, although he had never had an examination of the blood. From November, 1900, until September, 1901, he had several chills, followed by a rise of temperature, with pain in all the bones and in the lumbar region. At this time I discovered numerous æstivo-autumnal parasites in the blood.

History of the First Attack Complicated by Malaria. On September 4, 1901, the patient had a chill, and was admitted to the hospital. At this time an examination of the blood showed a few nearly full-grown tertian parasites and numerous æstivo-autumnal parasites. Patient appeared in fairly good condition, although somewhat anæmic. He presented a coated tongue, and complained of constipation, severe headache, and backache. Physical signs negative. The case at this time was supposed to be one of malarial fever, and quinine was given in large doses. The temperature at this time did not go above 102° F., and the treatment with quinine brought it down to normal in a few days, and the patient was returned to duty. On September 18th the patient had another chill, and was again put upon sick report. An examination of the blood at this time showed a few æstivo-autumnal parasites, and treatment with quinine was resumed. Patient complained of the same symptoms as in the previous attack, but mostly of severe pains in the joints. An examination of the blood was made every day, and the æstivo-autumnal parasites disappeared by the 21st, but the patient continued to run an irregular temperature. This irregularity continued, as will be seen by reference to the chart (Chart I.), until October 13th, during which time no malarial parasites could be demonstrated in the blood, and an examination was asked for as to

the possible occurrence of Malta fever. This examination was unsatisfactory because of the fact that my culture of the micrococcus melitensis had become infected, and it was impossible to secure a new one, It was noticed, however, that a partial agglutination was obtained. and from the history of the second attack I have no hesitancy in asserting that this continuation of the temperature after heroic doses of quinine was due to the presence of Malta fever. On reference to the chart it will be seen that the temperature shows a marked quotidian character, there being a daily rise and fall, much resembling that found in many cases of tuberculosis. The highest point reached at any time was 104° F., but most of the time the temperature did not go above 102° F.

The patient gradually convalesced, and was discharged from the hospital on October 19th, after a week's normal temperature. The symptoms complained of during the time in which the malarial parasites were absent from the blood were those of pain in the joints, a feeling of marked malaise, and considerable frontal headache. Patient appeared anæmic, the skin of a yellowish hue, and he became considerably emaciated. At this time he also suffered from a slight nephritis, as shown by an examination of the urine.

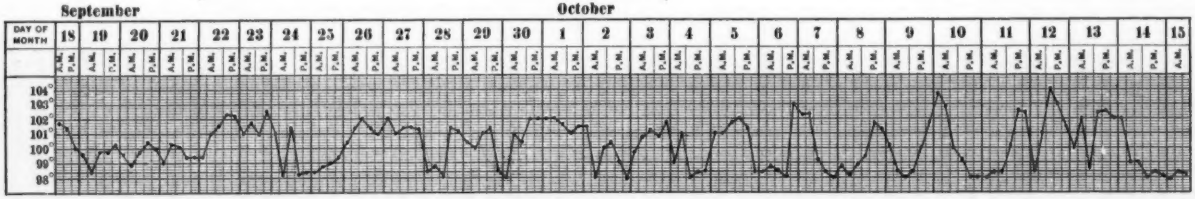
There can be no doubt, I believe, that this attack was due to Malta fever, but was complicated at its commencement by malarial fever, which soon succumbed to the influence of quinine, but which in no way affected the course of the Malta fever.

History of Second Attack. From October 19th to December 15th the patient remained comparatively well, although he complained at times of slight headache and chilly sensations, together with some pain, especially noticeable in the articulations. On the 15th of December he had a slight chill, and was readmitted to the hospital with a temperature of 100° F. An examination of his blood for ten consecutive days showed no evidence of malarial infection; but from the previous history of the case it was supposed that the temperature at this time was due to malaria, and large doses of quinine were administered. A request was not made for the Malta fever reaction until January 18th, at which time the temperature had reached normal. At this time the reaction was positive at once in a dilution as high as 1 to 250. This reaction was repeated several times, and was always found positive, and immediately cleared up the doubt which had attended the case from the commencement of the first attack.

The symptoms complained of during the second attack were similar to those of the first, there being marked pain in the joints, considerable headache, a furred tongue, and a markedly anæmic countenance. From a consideration of the chart of the second attack (Chart II.) it will be seen that the temper ature during this attack differed greatly from that of the first. During the first attack the temperature was markedly quotidian in character, while during the second the temperature stayed above normal for from five to seven days at a time.

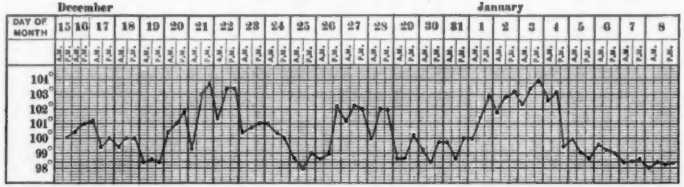
These two charts illustrate remarkably well the irregularities of the temperature in Malta fever during different attacks of the disease and of how comparatively little value the temperature chart is in these cases.

CHART I.



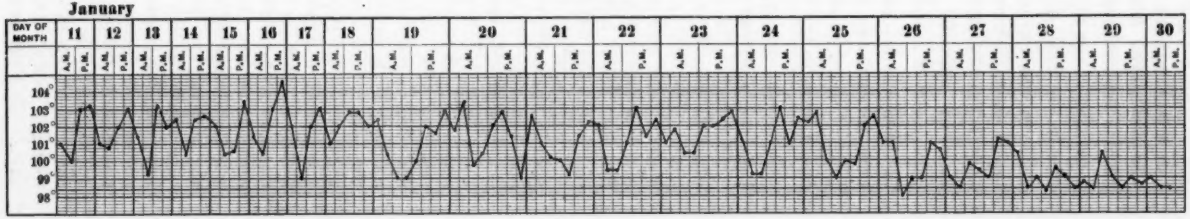
CASE I.

CHART II.



CASE I.

CHART III.



CASE II.

During the second attack the patient had no signs of nephritis, and this attack was not as severe or as long continued as the first. Patient was discharged from the hospital on January 19, 1902, having had a normal temperature for two weeks. Since that time there has been no repetition of the attacks, but he has complained considerably of stiffness in the joints and slight chilly sensations.

There can be no doubt but that this infection was contracted prior to the patient's arrival at this hospital, as he gives a distinct history of similar attacks in the Philippines, which were considered, however, of malarial character, the blood never having been examined. The occurrence of malaria, together with the first attack, further obscured the case, and led naturally to the inference that these attacks of fever were, in fact, due to malarial infection. This case shows the importance of blood examinations and the use of the agglutination test for Malta fever in the obscure fevers which are prevalent in the Orient.

Case II.—C. H. M., musician, Company "D," Twenty-seventh Infantry, aged twenty-three years; American.

History Previous to Admission. Patient gave but little history previous to admission save that of suffering from malaria in the Philippines. He had several attacks of slight chills, followed by fever, general pain, and severe headache while campaigning, and was diagnosed as a case of malarial cachexia. He was on sick report four or five days before admission to this hospital at the Presidio, complaining of pains in the left hypochondriac region.

History after Admission. On admission patient complained of severe pain in the lumbar muscles, tenderness upon pressure over the spleen, and headache. There was considerable cough present. Bowels were constipated, and there were some mucous râles heard at the base of the right lung. The patient had an irregular temperature previous to admission, and on January 7th had a distinct chill, the temperature reaching 103° F. An examination of the blood was negative for malaria. From this time the temperature stayed above normal until January 17th, as will be seen on referring to the chart (Chart III.). On the 14th a Widal test was requested, which was negative. At this time the temperature resembled that of typhoid fever very closely, although the patient had no symptoms referable to that disease, complaining mostly of pain in the back and slight headache. Upon the 16th of January a request was made for a Malta fever test, and a reaction was obtained almost immediately with a dilution of 1 : 100. This test was performed repeatedly afterward until the patient's discharge from the hospital, and was always positive. Upon referring to the temperature chart in this case it will be seen that the temperature curve is irregular, the temperature from January 7th to the 17th staying above normal and resembling that of typhoid; while after the latter date the temperature became more irregular, there being a daily remission, thus approaching the quotidian character shown in Chart I. The patient ran a temperature from January 7th until January 31st, and was then returned to duty after the temperature had remained normal for several days. This infection was undoubtedly contracted in the Philippines,

as the patient had been entirely well until his arrival in the islands, and there suffered from attacks which he said were similar to the present one. The chief symptoms complained of were muscular pain, especially prominent around the articulations, and slight headache. Bowels were constipated, and considerable anæmia developed during the attack.

CASE III.—J. M., sergeant, Fourth Infantry, aged twenty-four years; American. The history of this patient previous to admission to the hospital was that of slight malarial attacks in the Philippines. On conversation with the patient he said he had suffered from several so-called malarial attacks in the Philippines, lasting from one to three weeks, although they were treated vigorously with quinine. There can be no doubt that these attacks were not malarial in character, and were probably due to Malta fever.

Upon admission to the hospital the patient appeared in good flesh, but was somwhat anæmic. He complained of constipation, there having been no bowel movements for several days. Besides constipation there was some tenderness in the region of the gall-bladder, and the patient said that he had suffered severely from muscular pain in the lumbar region and pain in the joints. Physical signs negative. Patient was admitted to the hospital January 21st, and complained of constipation. At the time of admission the temperature was 102° F., but an examination of the blood did not show any malarial infection. On January 24th a request was made for a Malta fever test, and an immediate reaction was obtained, very marked, with a dilution of 1 to 100. This reaction was repeatedly confirmed during the patient's stay in the hospital. From January 21st to the 29th the patient ran a low temperature, never above 102° F., and generally between 101° F. and normal. He complained mostly of pain in the joints. The tongue appeared fairly clean. There were no physical signs whatever which could be considered characteristic. On February 5th the patient was discharged from the hospital, having had a normal temperature since January 29th. I have not reproduced the temperature chart in this case, as it is uninteresting, showing simply a low quotidian temperature curve entirely uncharacteristic. The case is of value, however, in showing the unreliability of the temperature chart in Malta fever.

CASE IV.—N. S. L., artificer, Fourth Infantry, aged twenty-three years; American.

History Previous to Admission. Patient suffered from repeated attacks of so-called malaria in the Philippines, having chills, severe muscular pain, and headache, these attacks lasting from one to two weeks. Patient's blood was never examined, but the attacks simulated those of malaria so closely that they were considered to be of that character. Quinine was given in large doses, but had no effect on the fever.

History after Admission. Patient was admitted to this hospital January 24, 1902, with a temperature of 103° F., and complained of severe headache, backache, and pain over the spleen upon pressure. There was a history of a decided chill. He appeared anæmic and jaundiced, and was constipated, and said that he had had similar attacks in the Philippines. An examination of the blood on the 25th was negative for malaria, but gave a marked reaction with the micrococcus melitensis in a dilution of 1:100. Patient's temperature reached normal on the 26th, although no quinine had been given, and remained normal

until February 4th, at which time the patient had a slight chill, the temperature reaching 103° F., and showing a quotidian character for a period of five days after. It remained normal until he was discharged, on the 19th. During this time the patient did not appear to be very sick, the only thing complained of being pains in the joints. The temperature chart is not reproduced, as it is not of special interest.

In considering the four cases noted it will be seen that the first two cases are those of acute exacerbations of Malta fever, in which the patient runs a temperature for a considerable length of time, while the latter two cases are characteristic of the chronic form of the disease, in which the temperature is but little above normal, and the chief symptoms present are those of articular rheumatism. Both of the latter cases would have been diagnosed as cases of articular rheumatism had it not been for the Malta fever reaction.

Methods of Performing Serum Tests for Malta Fever. The serum test for Malta fever was first described by Wright, of the Royal Army Medical School, at Netley. The methods of performing the test vary somewhat, but the principle is the same in all. He discovered that the serum of Malta fever cases had the power of agglutinating the micrococcus in suspension, and that this reaction took place earlier than the Widal reaction and in much more dilute solution.

Wright's Method. Sedimentation tubes having a diameter of less than 1 millimetre and an agar culture of the micrococcus are used in making the test. A salt solution suspension is made, and this solution is used to dilute the blood serum, the dilution varying according as the test is desired to be more or less delicate. It makes no difference whether the micrococci are alive or dead, the agglutination reaction taking place as well with one as the other.

Curry's Method. Curry's method of performing the test[1] differs somewhat from that of Wright, and is thus described by him: "I used common glass tubing about 3 to 4 mm. in diameter, and made the observations macroscopically, and as a control made microscopic observations of drops of the fluid withdrawn by means of a platinum loop from the top, middle, and bottom of the tube. Tubes 7.5 cm. long and 3 to 4 mm. in diameter were made from glass tubing, and the bottoms were drawn out to a long, sharp point. These were sterilized and plugged with cotton in the dry sterilizer. Salt solution suspensions were made according to the method used by Wright. Bacteria were killed by heat at 60° C. for fifteen minutes, and 0.5 per cent. carbolic acid added. As a routine method one drop of blood serum was mixed with nineteen drops of normal salt solution, then equal parts of this mixed with the salt suspension of the culture of the micrococcus melitensis and placed in the small tubes of the sterile pipette. This equals

[1] "Malta Fever," Journal of Medical Research, vol. vi., No. 1.

a dilution of 1 to 40. A reaction was called positive and complete only when, in addition to the precipitation of the bacteria in the bottom of the tube, the supernatant fluid became clear.

Author's Method. In performing the serum test for Malta fever I have used practically the same method as that used for making the Widal test. A pure culture of the micrococcus, either upon agar or in bouillon, was used. The test may be performed either with the fresh serum or with a dry drop of blood, the latter being used preferably, as it is simpler and easier to procure. A drop of blood is secured upon a glass slide and diluted with enough sterilized water to dissolve it. A graduated pipette of very small calibre is used to make the dilution with the micrococcus. Having dissolved the drop of blood, a known portion is taken from it by the pipette and placed upon a clean slide; this is then diluted with a measured quantity of the bouillon culture or with a suspension of the agar culture made with sterilized water. The pipette is so graduated that a dilution can be made from 1 : 10 to 1 : 150. A cover-glass is then placed over the mixture, and this examined microscopically. In using the agar suspension the drop should first be examined so as to be sure there is no agglutination present before the blood is added. Preferably I have used a dilution of 1 : 75, although the agglutination reaction has been obtained with dilutions as high as 1 : 250 immediately. This method is easy of performance, all that is needed being the culture, the special graduated pipette, the cover-glass and slides, and the drop of blood. The method was used in all the cases described, and controls with a serum of other diseases—such as typhoid, dysentery, etc.—made at the same time, and it was found perfectly reliable.

LITERATURE. The literature concerning the appearance of Malta fever among the soldiers of the United States army is very limited. The first case described was that of Dr. Musser, of Philadelphia, in the *Philadelphia Medical Journal* December, 1898. His case was that of an officer who contracted the disease in Porto Rico, and he was the first to draw attention to the fact that the disease was probably endemic in that island.

In the *Report of the Surgeon-General of the Army for 1899*, Walter Cox described a case occurring in Porto Rico and observed by him. The patient was a private of the Hospital Corps, aged thirty years. He came under observation January 14, 1899. He contracted fever in the guard-house of an old Spanish barracks, the fever commencing January 11, 1899. He complained of pain all over the body, especially in the bones and joints. Had two chills on successive days, but none afterward. This was at the commencement of the illness. The appetite was poor, and the bowels were at first loose and later constipated. The temperature curve showed daily remissions and reached normal

gradually. The morning temperature for a considerable time reached the normal point, but was 1, 2, or 3 degrees above normal toward evening. He was discharged from the hospital on April 3d, after about a week of normal temperature, but was readmitted April 7th, suffering again from fever. This attack was similar to the first. The blood was examined repeatedly for the malarial parasites as well as for the Widal reaction. A test with a culture of the micrococcus melitensis showed a marked agglutination in dilutions as high as 1 : 60.

Chamberlain, while on duty on the hospital ship "Relief," at Manila, P. I., observed two cases of the disease in soldiers, which were reported to the Surgeon-General of the Army. The men were in adjacent beds, and both presented mild attacks. The temperature curve was irregular, being neither markedly remittent nor undulating. The cases were first diagnosed as malarial fever, but the Malta fever reaction was performed at the laboratory of the First Reserve Hospital, and both were found positive. Examination of the blood for malarial parasites and the use of the Widal test both resulted negatively.

Curry and Strong, in 1900, reported cases occurring at the First Reserve Hospital. Strong performed an autopsy upon a man who had died from a continued fever of long duration. The post-mortem showed that it was neither typhoid nor malaria, and cultures from the case made by Curry resulted in the finding of the micrococcus melitensis. Inoculations into monkeys produced the typical symptoms of Malta fever. While performing these experiments Strong became infected and suffered from a typical attack of the fever. In another case the condition was discovered post-mortem, and cultures were obtained of the micro-organism. At this time two cases were observed in the wards of the hospital which gave the reaction with the micrococcus, and were undoubtedly cases of Malta fever.

The most valuable report of Malta fever occurring in soldiers of the army is that written by Curry and published in the *Journal of Medical Research*, vol. vi., No. 1. In this report Curry describes the cases which have come under his observation both in Manila and in the Army and Navy General Hospital, at Hot Springs, Ark. Besides the four cases of Malta fever observed in Manila, he observed in all eight cases of Malta fever in the hospital at Hot Springs. Four of these are described *in extenso*, the notes of the other four cases occurring in a note at the end of the report. All four of the latter cases were in a convalescent stage, the prominent symptoms being those of articular rheumatism, constipation, and frequent profuse sweatings. These cases were all diagnosed as articular rheumatism. Of the four cases described more fully all gave a marked serum reaction with the micrococcus melitensis when in a dilution as high as 1 to 300. None of the cases presented the symptoms found in the acute stage. The

symptoms complained of were pain in the articulations, constipation, and sweating, and all showed anæmia. These cases were all supposed to be suffering from chronic articular rheumatism.

In his recapitulation Curry says: "We have four cases of what was thought on admission to be chronic rheumatism. These cases have not improved under treatment nor by change to this favorable climate. Neither antirheumatic nor antimalarial treatment has benefited these men. In spite of treatment and favorable conditions, repeated and more or less regular recurrences of acute rheumatic pains and swellings and of fever have taken place. These conditions have lasted a long time—from six months, the shortest, to sixteen months, the longest of the series. The other prominent symptoms have been anæmia, profuse sweatings, and constipation. The blood examinations for malarial fever and for typhoid were negative, save in the case of one who had had severe typhoid fever two years ago. The clinical history of these cases corresponds with that of Malta fever, and the result of the serum test with the micrococcus makes it certain that the diagnosis of Malta fever in these cases is a correct one."

The important lesson to be learned from a study of the literature of Malta fever occurring in the United States army, and from the study of the cases described in this report, is that the condition is one not easily recognized clinically, and one apt to be mistaken for typhoid, malaria, or, in the chronic stage, for articular rheumatism. This being so, the great value of a microscopic examination of the blood and the performance of the serum test is at once proven. None of the cases observed by me was diagnosed as Malta fever, and in only one of them was there any suspicion of the occurrence of this disease. The two cases presenting the chronic symptoms would, in all probability, have been transferred to Hot Springs, Ark., for antirheumatic treatment, while in the two cases presenting the acute symptoms the patient would probably have been treated for either malaria or typhoid fever. In fact, in Case I., on account of finding malarial parasites at different times in the patient's blood, the treatment had been altogether that for malaria; and had a diagnosis of Malta fever been made more quickly much discomfort would probably have been saved the patient. The following conclusions may be drawn from the study of these cases:

1. There occurs in the tropics and subtropics a fever which may resemble in its acute stage either typhoid or malaria, and in its chronic stage articular rheumatism, caused by the micrococcus melitensis.

2. There are no pathognomonic symptoms of Malta fever. The symptoms observed are so inconstant and confusing that no one of them can be said to be typical of the disease.

3. A differential diagnosis of this fever is almost impossible in the majority of cases without the aid of the microscope and the serum test.

ON MULTIPLE SEROSITIS—THE ASSOCIATION OF CHRONIC OBLITERATIVE PERICARDITIS WITH ASCITES, WITH PARTICULAR REFERENCE TO THE "PERICARDITIC PSEUDOCIRRHOSIS OF THE LIVER" OF PICK AND THE "ICED LIVER" (ZUCKERGUSSLEBER) OF CURSCHMANN.[1]

By Aloysius O. J. Kelly, A.M., M.D.,
of Philadelphia,
Instructor in Clinical Medicine, and Assistant Physician to the Hospital, University of Pennsylvania; Pathologist to the German Hospital of Philadelphia; Professor of the Theory and Practice of Medicine, University of Vermont, etc.

For purposes of study, cases of chronic adhesive or obliterative pericarditis may be divided into three classes: first, cases in which the pericarditis runs its course entirely devoid of symptoms and constitutes merely an accidental though interesting finding at the necropsy; second, cases in which, sooner or later, symptoms of disturbed or impeded cardiac action manifest themselves, and in which, from the physical signs, the obliterative pericarditis is more or less susceptible of diagnosis; and, third, cases characterized clinically by marked ascites, with little or no œdema of the legs, cases in which the diagnosis of cirrhosis of the liver is usually made and which at the necropsy reveal chronic obliterative pericarditis and certain morbid changes in other tissues and organs—notably pleuritis, peritonitis, perihepatitis, nutmeg liver, red atrophy of the liver, cirrhosis of the liver, etc. It is to the third class of cases that I wish to direct attention.

In the majority of cases when chronic adhesive or obliterative pericarditis gives rise to symptoms, the symptoms that arise are those of failing cardiac compensation—palpitation of the heart, dyspnœa, cough, cyanosis, generalized œdema, effusions into the several serous cavities of the body, etc. On the contrary, in the cases that simulate cirrhosis of the liver, clinically, the first symptoms are sensations of fulness, oppression, and weight in the upper abdomen, or there may be apparently a sudden onset with acute pain; the abdomen increases in size and may attain very large dimensions—due evidently to ascites that may necessitate repeated tappings (Rumpf's patient was tapped 301 times).

With increase in the amount of the ascites the abdominal walls become tense and painful, and the other subjective symptoms become

[1] Read, by invitation, at a meeting of the Johns Hopkins Hospital Medical Society, Baltimore, and at a meeting of the College of Physicians of Philadelphia.

markedly aggravated. There may be slight and transitory jaundice. Later œdema of the legs may develop. In a few cases œdema of the legs comes on early; it may remain but a short time, disappear, and not recur until shortly before the death of the patient. In rare cases it persists; but in the class of cases to which I refer it is always inconspicuous when contrasted with the excessive and constantly recurring ascites, and it scarcely attracts attention.

This symptom complex of obliterative pericarditis is of uncommon occurrence. While by no means unknown to the older writers, it attracted but little attention, and it was not until the communication of Pick, in 1896, that it became the subject of much discussion. Even at the present time it is overlooked by a number of systematic writers on diseases of the heart and of the liver, and a search through a number of recent text-books on medicine reveals little or no mention of it.

In the present state of our knowledge, it is to some extent a matter of personal opinion what cases should be included in the group of cases under discussion. From the point of view that I hope to elaborate, the earliest recorded case that I should include within this group was reported by van Deen in 1846. Subsequently cases were reported by Frerichs, Feierabend, Hambursin, Weiss, Vierordt, Tissier, Hirschler, Weinberg, Mott, Variot, Riedel, Henoch, Harris, Broadbent, and Dickinson. In 1884 Curschmann described his now well-known "zuckergussleber," or chronic hyperplastic perihepatitis—a disease characterized by a slow, insidious, and intermittent course, and persistent ascites, but without connective tissue hyperplasia in the liver. Although usually described as the "zuckergussleber" of Curschmann, this chronic hyperplastic perihepatitis was well known to a number of the earlier writers, being described by Hilton Fagge, in 1875, by Wilks and Moxon, in 1875, by Murchison, in 1868, by Bamberger in 1864, and by Rokitansky, in 1842. In 1895 a paper on the same subject, with the report of a case, was published by Rumpf. In 1896 Pick, reporting three cases, directed attention to the symptom complex simulating that of cirrhosis of the liver, but found at the necropsy to be due to obliterative pericarditis and associated changes in other tissues.

Pick pointed out that the recurring ascites with almost entire absence of œdema of the legs, the enlarged, firm, and somewhat irregular liver, and absent or slight jaundice, strongly suggested cirrhosis of the liver, and that the obliterative pericarditis usually escaped clinical recognition—although he was enabled to make the correct diagnosis during life in the third of his reported cases. Pick suggested for these cases the designation "pericarditic pseudocirrhosis of the liver"—a designation that has since found favor with some medical writers, and he

endeavored to establish an etiological relationship between the obliterative pericarditis, the enlarged liver, and the ascites. He stated that as a consequence of the pericarditis, which he looked upon as the primary disease, disturbances of circulation, with consecutive connective tissue hyperplasia in the liver, occurred, and that as a result of these ascites developed. In this class of cases he included the cases of "zuckergussleber" previously reported by Curschmann and by Rumpf, Following Pick's paper, the subject attracted considerable attention, reports of a number of cases appeared, discussions relating to the nature and the sequence of the morbid processes arose, and the interpretations of the lesions were many. Mention may be made of the papers by Heidemann, Hübler, Siegert, Werbatus, Nachod, Taylor, Ewart, Diemer, Schmaltz and Weber, Rose, Eisenmenger, Pick, Giradeau, Rosenbach, Hutinel, Türk, and others.

A disease that is identical with that under discussion has been well recognized in Italy, being known in some quarters as Concato's disease, polyorrhomenitis, or polyserositis. In 1891 Picchini published an extended report of the disease—basing his remarks upon personal observations and a critical study of the cases reported in the literature. Interesting papers were published by Cantu in 1894, and by Villani in 1895.

In 1898 Hager, a German author, writing on the subject, reviewed critically the Italian literature. Since the publication of Pick's paper, papers by Schupfer, Bozzolo, Galvagni, Patella, Caporali, and others have appeared. In France the disease is sometimes known as perivisceritis.

The only reports of cases by American writers that I have been able to find are those by Osler, in 1896, by Cabot, in 1898, and by Herrick, in 1902.

The subject has not been entirely neglected by systematic writers. Thus, in 1887, Rosenbach stated that pericardial obliteration is sometimes associated with extensive fibrous perihepatitis, enlargement of the liver, and ascites, "so that one might presume that enlargement of the liver, ascites, and pericardial synechiæ stand in causal relationship the one to the other." He refers to the subject also in his book on diseases of the heart. In 1890 Strümpell wrote that in cases of pericardial obliteration, he, as well as others, had sometimes observed marked ascites (at times associated with hydrothorax) without coincident œdema of the legs. In the latest edition of his text-book on medicine, referring to the subject, he states that all the cases presenting the symptom complex under discussion are not of one nature. In 1891 Leube wrote that pericardial obliteration sometimes gives rise to swelling of the liver and consequent ascites. In 1894 Schrötter wrote that pericardial obliteration sometimes gives rise to ascites before the occurrence of

general anasarca. The subject was referred to also by Osler, in the second edition of his text-book on *Practice of Medicine*, in 1895, by Quincke and Hoppe-Seyler, in 1899, and by Roberts, in 1900.

The subject may be illustrated by the report of the subjoined case. For the clinical notes, I am very much indebted to Dr. James C. Wilson, physician-in-chief, and to Dr. John B. Deaver, surgeon-in-chief, to the German Hospital.

Henry S., single, white male, aged thirty-one years, a native of Sweden, and a clerk by occupation, was admitted to the medical wards of the German Hospital, May 31, 1898, and the following history elicited:

He is the only child of his parents, both of whom are living and well. He has no knowledge of his having had any of the diseases of childhood. From an early age, however, he had been subject to convulsive seizures attended with unconsciousness. It is reported that his mother was similarly affected. The spells, as they occurred in the patient, came on at irregular intervals and lasted for from several minutes to about an hour. When about sixteen years of age they increased very much in frequency. At times he had a premonition of their oncoming. During some of the lighter attacks he did not lose consciousness entirely, that is, he was more or less aware of what was transpiring about him, but he was unable to speak. When about eight years of age he had severe pains in both groins and in the upper part of both thighs. At times these were so severe as to prevent his lying down.

At about the same time he experienced paræsthetic phenomena in the rectum—he felt as though there was something creeping about in the rectum. At the age of eighteen years he acquired gonorrhœa. One year later he had a severe attack of rheumatism that lasted about three months. Since then he has had a number of minor attacks of rheumatism, but none was severe enough to disable him. In 1890 he was treated in Bellevue Hospital, New York, for what he states was malaria. (A note from the Medical Superintendent of Bellevue Hospital, under date of March 12, 1901, states that the patient was treated in the hospital for malaria, from July 13 to 18, 1890. No details of his condition at that time are available.) For a short time during 1892 the patient was confined to an asylum. He had suffered a sunstroke and had become, he states, maniacal at times. Since then he has been troubled with disordered digestion, or "stomach trouble," as he expresses it. Although he is said to have been jaundiced at times, the most obtrusive symptom has been periodic pains in the right half of the abdomen just above the right iliac fossa. These occurred at first at intervals of about a month, later at intervals of two months or more.

During April, 1898, the patient was in the Jefferson Medical College Hospital for about two weeks. (Through the courtesy of Dr. H. A. Hare, I have ascertained that while in the hospital the patient was slightly jaundiced, and at times delirious, that he had several convulsions, and that although he complained of severe pain in the right upper abdominal quadrant and of tenderness over the region of the

gall-bladder, careful examination under ether failed to reveal any tumor in the region of the gall-bladder or other evidences of gallstones. The liver was slightly enlarged, and the superficial veins, especially those on the right side of the abdomen and the inner side of the right thigh were distended. The urine at this time was acid in reaction, had a specific gravity of 1025, contained 3.2 per cent. of urea, and neither sugar nor albumin. Examination of the blood revealed: erythrocytes, 5,200,000; leucocytes, 24,000; and hæmoglobin, 73 per cent. A differential count of the leucocytes revealed: small lymphocytes, 4 per cent.; large lymphocytes, 5 per cent.; transitional leucocytes, 4.9 per cent.; polynuclear leucocytes, 85.1 per cent.; and eosinophiles, 1 per cent.) Shortly after leaving the Jefferson Medical College Hospital the patient's abdomen began to enlarge, the pains in the right side of the abdomen became more severe and more frequent, so that he was incapacitated for work. He was admitted to the German Hospital complaining of severe pain and tenderness in the right upper abdominal quadrant, especially over the region of the gall-bladder, which was aggravated by deep inspiration; of pain over the pubes after micturition; at times of general pain in the right side of the abdomen; sharp cutting pains about three inches within the anus; attacks of vertigo; spots before the eyes; and of constipation of three years' duration. He smokes moderately, and formerly he consumed considerable quantities of alcohol.

On examination the only noteworthy sign was marked distention of the abdomen, due evidently to ascites. His liver dulness extended upward to the third rib. On June 2 the patient's abdomen was tapped, and 4400 c.c. of clear amber fluid was withdrawn. The fluid had a specific gravity of 1015, and contained a few erythrocytes and many leucocytes. The tapping relieved the patient very much, and afterward the liver dulness was found to be normal in area. There was marked tenderness over the region of the gall-bladder. Examination of the blood, on June 3, revealed the following: hæmoglobin, 82 per cent.; erythrocytes, 3,930,000, and leucocytes, 7300. A differential count of the leucocytes revealed the following: small lymphocytes, 11 per cent.; large lymphocytes, 9 per cent.; transitionals, 3 per cent.; polynuclear neutrophiles, 76.5 per cent., and eosinophiles, 0.5 per cent. On June 13 it was noted that the ascites was gradually reaccumulating, and the pains were becoming more frequent and more marked. On June 22 the patient was again tapped and 6700 c.c. of clear amber fluid was withdrawn. The fluid had a specific gravity of 1018, and contained a few erythrocytes and many leucocytes. On July 2 it was noted that the pain in the region of the gall-bladder had been absent since the second tapping. On this date the patient's feet were found to be slightly swollen—the first swelling of the feet since he had been in the hospital. (Upon inquiry he admitted that they had been slightly swollen on one previous occasion.) On July 9 the patient felt better than he had during the previous six months, and he was free from pain. On August 9, feeling well, he left the hospital of his own accord. His feet were not swollen at all, and he suffered no pain. His abdomen, however, contained considerable fluid, and was greater in circumference than it was when he entered the hospital. On the second day after his admission to the hospital his temperature was 102° F., and on several occasions subsequently it reached 100° F. Otherwise there was no

fever. His pulse was always low: on several occasions it was 80 per minute; usually it was between 60 and 68; and sometimes it was as low as 48 per minute. His urine was normal.

The patient was readmitted to the German Hospital, June 23, 1899, complaining of marked distention of the abdomen, pains in the region of the liver, at times of sharp shooting pain in the perineum, dyspnœa, slight pretibial œdema, diminution in the amount of urine voided daily, vertigo, and spots before his eyes. He stated that since he left the hospital his abdomen had been tapped twice. Inasmuch as the clinical diagnosis was cirrhosis of the liver, operation for the relief of the condition was proposed and acceded to by the patient. The operation was performed by Dr. John B. Deaver, July 3, 1899. In brief this consisted in irritating the peritoneum and stitching the omentum to the parietal peritoneum. The patient survived the operation four days, dying July 7, 1899.

The following are the notes of the necropsy performed by myself, July 8, 1899:

The body is that of a well-developed, fairly well-nourished male subject, with good bony development, good musculature, and moderate panniculus adiposus. There is post-mortem lividity in the dependent portions of the body; the skin is slightly jaundiçed; there is no œdema of the extremities. In the median line of the abdomen there is a wound, about 16 cm. in length, apparently healing by first intention. The left pleural cavity is entirely obliterated by firm adhesions—the two layers of the pleura being dull, cloudy, whitish, and thickened. The left lung is about normal in size, and mottled grayish-black in color. Its air content is normal, its consistency firm, and it shows some hypostatic congestion in the dependent portions. Its section surface is smooth, moist, glistening, dark reddish in color, and exudes a quantity of frothy, blood-stained fluid. The lung crepitates throughout, and contains no tubercles. The bronchi are normal in size, they contain a small amount of mucus, and their mucous membrane is pale. The pulmonary vessels and the peribronchial lymph glands appear normal. The right pleural cavity is entirely obliterated by firm adhesions—the two layers of the pleura being dull, cloudy, whitish, and thickened. The right lung presents appearances similar to its fellow. The pericardium is firmly adherent to the anterior chest wall and the adjoining mediastinal tissues. The pericardial cavity is entirely obliterated, and such is the firmness of the adhesions that the two layers of the pericardium nowhere can be distinguished. In addition the pericardium is the seat of extensive calcareous infiltration, a large section of the heart being encased in a hard calcareous sheath. This calcareous sheath implicates the pericardium of the right ventricle, about one-half of the anterior and under surface of the right auricle, the left edge of the heart, the lowermost two-thirds of the left ventricle, the apex, and the diaphragmatic surface of the heart. This calcareous sheath appears to be made up of a single calcareous plate and not of a series of disunited plates. The pericardium of the left auricle, though firmly united with the adjacent parietal pericardium, is not the seat of calcareous infiltration. The several cavities of the heart appear to be normal in size, and they contain a moderate amount of dark, reddish-

brown, coagulated blood. The mitral orifice admits two fingers, the tricuspid orifice, three fingers. The mitral and tricuspid valve leaflets and the associated chordæ tendineæ are slightly thickened. The aortic and pulmonary valve leaflets are normal. Presumably all the valves are competent. The left ventricle (including the calcareous pericardium) measures 12 to 14 mm. in thickness, the right ventricle 5 to 8 mm., the left auricle 2 to 4 mm., and the right auricle 2 to 4 mm. The heart muscle is reddish-brown in color and firm in consistency. The coronary arteries and the aorta are normal. The heart and pericardium weigh 470 grammes. The omentum is normal in size and shape. The entire peritoneum is dull, lustreless, somewhat thickened, and intensely hemorrhagic. The coils of intestine are united to one another and to the other intra-abdominal organs by moderately firm, though friable, fibrinous adhesions. In some places an exudate may be stripped off in thin layers. The peritoneum contains also about 50 c.c. of serosanguinolent fluid (drainage had been provided at the time of the operation). The liver is firmly united to the under surface of the diaphragm by means of dense and firm adhesions, especially for a distance of about 6 cm. on both sides of the suspensory ligament. The capsule of the liver is thickened throughout, but especially on its upper surface, where in some places it is 4 mm. thick. In addition, on the capsule of the liver there is some fresh fibrinous exudate that may be stripped off; this is present especially on the under surface of the liver and for a short distance on the upper surface. The liver measures 22 cm. in length, 14 cm. in breadth, and 9 cm. in thickness. It weighs 1460 grammes. Its shape is normal, its consistency somewhat increased, its elasticity somewhat diminished, its surface somewhat irregular, and its edges rounded and hard. Its section surface is dull, moist, slightly granular, opaque, and light reddish-brown in color. The liver lobules are distinct, and there appears to be a slight increase in the connective tissue of the organ. The gall-bladder is normal in size and contains fluid bile. Its mucous membrane and wall are normal. The cystic, hepatic, and common bile-ducts are patulous. The spleen measures 10 cm. in length, 8 cm. in width, and 5 cm. in thickness. It is normal in shape and weighs 210 grammes. It is firm in consistency, and its capsule is slightly thickened and covered also with some fresh fibrinous exudate. The pulp is normal, the follicles rather distinct, and the trabeculæ slightly increased. The right kidney measures 11 cm. in length, 6 cm. in width, and 3 cm. in thickness. It is normal in shape and weighs 160 grammes. Its capsule strips readily, its surface is smooth, its color dark reddish-brown, and its consistency somewhat increased. The cortex is 7 mm. thick, and dark reddish-brown in color; the pyramids are congested. The calyces, pelvis, and ureter are normal. The left kidney weighs 170 grammes, and presents appearances similar to its fellow. The adrenals are normal. The bladder contains a small quantity of clear urine; its mucous membrane and wall are normal. The stomach is normal in size and position. It contains some turbid brownish fluid. The mucous membrane is congested and somewhat swollen. The duodenum and the remainder of the intestine are normal. The brain and spinal cord were not examined.

The anatomical diagnosis was as follows: acute hemorrhagic peritonitis; chronic adhesive pericarditis, with extensive calcification; chronic bilateral adhesive pleuritis; chronic perihepatitis (pericarditic

pseudocirrhosis of the liver of Pick); slight congestion of the liver, spleen, and kidneys.

Microscopic examination of the thickened pericardium revealed marked overgrowth of fibrous connective tissue with relatively few cells, and some extension of the newly-formed connective tissue into the interstices of the heart muscle. Careful examinations of sections from several regions revealed no evidences of tuberculosis. Examination of the thickened pleuræ revealed only fibroid thickening; no evidences of tuberculosis. Examination of the liver revealed chronic fibroid thickening of the capsule and some slight extension of connective tissue trabeculæ a short distance into the substance of the liver. In addition, evidences of acute inflammation were apparent, the round-cell infiltration being rather abundant. No evidence of tuberculosis could be detected. The liver itself revealed moderate distention of the central veins of the lobules and of the adjoining capillaries, with a moderate atrophy of the intervening liver cells. The cells of the periphery of the lobules showed slight fatty infiltration. The interlobular connective tissue possibly was slightly in excess of the normal, and contained a slight amount of round-cell infiltration. The spleen revealed the usual evidences of slight congestion and slight thickening of the trabeculæ.

The occurrence of marked ascites, with little or no œdema of the extremities in cases of failing cardiac compensation, though not very common, is by no means unknown. It was mentioned by Liebermeister in 1864, by Oppolzer in 1866, and it is observed by most clinicians of experience at the present time. The difficulties attending the diagnosis in these cases, however, are sometimes very great. The question whether an enlarged liver (in advanced cases a small liver) with ascites is to be referred to a primary or a secondary liver disease, if it presents itself to the mind of the clinician at all, may be difficult of solution. Light is shed on the case by the detecting of trustworthy evidence of cardiac valvular disease—in which case, especially if the patient be an adult, one has to determine whether the liver condition and the ascites are due to the heart disease or to an associated alcoholic cirrhosis of the liver. The diagnosis is even more difficult in cases of obliterative pericarditis, which appears to give rise to disproportionate ascites more frequently than does valvular disease of the heart. In these cases the pericarditis being usually latent and more or less insusceptible of diagnosis, the ascites is generally referred to a cirrhosis of the liver, rarely to tuberculous peritonitis, etc.

The cause of disproportionate ascites in cases of obliterative pericarditis has occasioned much discussion. Thus Weiss attributed it to changes in the bloodvessels of the peritoneum, the result of chronic peritonitis. He believed that in consequence of the pericardial obliteration general venous congestion occurs; that in consequence of the inflammation of the peritoneum, the peritoneum becomes a punctum minimæ resistentiæ; that transudation of serum occurs more readily from the altered vessels of the peritoneum than from other vessels of the body;

and that in consequence of the development of the ascites venous congestion in other parts of the body is relieved, and the development of œdema more or less prevented.

Mott believed that owing to the adherent pericardium interfering with the coronary circulation, the heart, instead of undergoing compensatory hypertrophy, as it sometimes does in the condition under discussion, slowly undergoes degeneration, and that this is doubtless hastened by the immense loss of fluid. He stated that, moreover, the thick adherent pericardium would interfere considerably with the elasticity of the walls of the heart and greatly modify its action as a suction pump during diastole, and that the circulation that this would affect most would be the portal, because here the blood has to pass through two sets of capillaries and against gravity. This is a view that is scarcely tenable, since, were it true, we should expect predominating ascites in all cases of failing cardiac compensation.

Weinberg attributed the ascites, with little or no œdema of the legs, to angulation of the inferior vena cava or the hepatic vein due to a right-sided pleural effusion. He assumed that in consequence of the angulation of the veins congestion and other changes in the liver, with consecutive ascites, occurred; and he endeavored to support his opinions by citing the results of some experiments of Rosenbach's that appeared to show that such right-sided pleural effusion may cause angulation of the vena cava and congestion of the portal area. However, as pointed out by Pick, it is difficult to conceive of isolated compression of the hepatic vein, and compression or angulation of the inferior vena cava results in œdema of the legs rather than in ascites. Furthermore, in many of the cases there is no right-sided pleural effusion.

Rosenbach, while scarcely venturing to express a positive opinion on the subject, states that the ascites cannot be the result of simple insufficiency of the heart muscle, and he attributes considerable importance to the fibrous alterations in the liver capsule. He says, further, that the ascites must be the result of the operation of special conditions which, though associated with the heart affection, are not the direct result of diminution of the power of the heart; and that probably we have to do with an extension of the inflammatory process from the pericardium along the large veins to the serous covering of the liver, or vice versa, with the final development of connective tissue hyperplasia.

Pick, criticising adversely the opinions of Weiss, Mott, and Weinberg, points out that each of these writers in attempting to explain the occurrence of the ascites entirely overlooked that organ which, from the clinical course of the disease, one would be inclined to think most at fault—the liver. He states that in these cases the liver is described as rounded, increased in consistency, hemorrhagic, enlarged, markedly

irregular, granular, very firm, cirrhotic—in short, the appearances of the different stages of cyanotic induration, atrophic nutmeg liver, or the cardiac cirrhosis of the French. And inasmuch as other writers have observed prevailing ascites rather than œdema of the extremities in certain forms of heart disease, with similar secondary changes in the liver, he prefers to attribute the ascites in these cases of obliterative pericarditis to the alterations in the liver rather than to assume certain hypotheses. He says, further, that the question why in these cases ascites rather than generalized œdema occurs is intimately bound up with the question why in certain cases of congestion of the liver, in failing compensation of the heart in valvular disease, connective tissue proliferation occurs, whereas in other cases it does not occur; and that concerning this we know little definitely. For the time being he was content to point out the diagnostic features of the symptom complex in question. He believes that the associated peritoneal alterations are more or less accidental—that the thickening of the peritoneum results from the long-continued congestion and the persistence of the ascites, and that the thickening and the adhesions are in part due also to infection the result of repeated tappings.

Harris states: "There are two lesions, either of which may possibly occur as complications to the mediastinal and pericardial affection, and which could explain the ascites in such cases. In the first place, it is conceivable that chronic venous congestion of the liver produced by the cardiac dilatation may in some cases set up a chronic inflammation of the liver, a secondary periportal cirrhosis, which like the ordinary alcoholic cirrhosis would obstruct the portal circulation and produce ascites. We have seen that an increase of fibrous tissue in the liver is found in some of the cases of mediastino-pericarditis; but such a change does not appear to be the rule, and in the cases where it has been found it is questionable whether it has been sufficiently pronounced to produce portal obstruction and ascites therefrom. Furthermore, in one of my cases (Case II.) where the abdominal dropsy was such a prominent feature of the illness, the ascites was certainly not due to a cirrhotic liver, no marked periportal cirrhosis being found on microscopic examination. The second explanation of the occurrence of the ascites in the cases under consideration is that a chronic peritonitis ensues, and to it the ascites is due. Such chronic peritonitis in some instances may possibly be an independent affection, and one not directly connected with the mediastinal or pericardial lesion; in other cases it is conceivable that the chronic venous congestion due to the intrathoracic affection sets up the chronic peritonitis. Such a chronic peritoneal change was found in my second case, and was clearly sufficient to account for the ascites. That it is the explanation of the ascites in all such cases, of course, we do not say. It is quite possible that other

complications may, in some cases, occur which account for the development of ascites as a prominent feature of the case." After further discussion of the question, he says: "I am inclined, therefore, to think that the ascites which sometimes occurs in cases of mediastino-pericarditis, and which is unaccompanied by extreme anasarca of the lower extremities, is due, in some instances, at all events, to the onset of a peculiar form of chronic peritonitis. This chronic peritonitis may be possibly due to venous engorgement of the peritoneum consequent upon the dilatation of the heart or venous obstruction in the mediastinum, or it may occur so early in the case as to be probably independent of such venous stasis. In my second case the ascites was a prominent symptom from a very early period of the illness, and probably was independent of venous engorgement, which only appeared as a marked feature some time after the development of the ascites."

Heidemann, supporting the opinion of Weiss, states that in these cases we have to deal with a chronic inflammation of divers serous membranes; that the congestion, the result of the degeneration of the muscle of the heart, leads to ascites because the vessels of the peritoneum, on account of the chronic inflammation, constitute a locus minoris resistentiæ; that the associated cirrhotic processes in the liver observed in these cases result from an extension of the inflammatory irritant from the liver capsule and from the chronic congestion of the organ; and that in consequence of proliferation and shrinkage of the connective tissue on and in the liver the congestion and exudation into the peritoneal cavity are increased.

Eisenmenger, a pupil of Paltauf, states that it is quite true that in consequence of obliterative pericarditis marked ascites, with little or no œdema of the legs, occurs comparatively frequently, and that if the pericarditis is latent, the symptom complex bears a certain resemblance to cirrhosis of the liver. He states further that this symptom complex is not due, as is asserted by Pick, to connective tissue proliferation the result of disturbances of circulation in the liver, but that in different cases it is due to different causes. He emphasizes the etiological importance of distortions, compression, and angulations of the inferior vena cava, produced by a concomitant exudate or pleuropericardial thickenings; concomitant peritonitis in the transverse fissure of the liver; and, because the symptom complex is observed especially in young persons, the condition of the capillaries and small vessels in healthy young persons, in consequence of which œdematous transudations occur readily. Inasmuch, then, as the disease is not an anatomical entity, he disapproves of the designation "pericarditic pseudocirrhosis of the liver," suggested by Pick.

Without detailing the opinions of other writers, it suffices to state that the opinions of Mott and Weinberg are scarcely worthy of serious

consideration. In addition to the opinion of Eisenmenger, which is not supported by the report of any illustrative cases, there remain three opinions held by as many different groups of writers: the first, represented by Pick, Bozzolo, Nachod, Galvagni, Cabot, and others, attributes the ascites to changes in the liver the result of long-standing congestion; the second, represented by Weiss, Heidemann, Schupfer, Werbatus, and others, attributes the ascites primarily to the chronic peritonitis; and the third, represented by Harris, Osler, Patella, Siegert, and others, attributes the ascites to the combined action of both of these factors.

In view of these differences of opinion, it may not be unprofitable, from a study of the cases reported in the literature, to ascertain the more likely cause of the predominating ascites, and in general the nature of the disease in question. From the subjoined table I have omitted all cases in which the ascites was merely a part of generalized dropsy and effusions into the several serous cavities of the body; cases, of which Wagner's and Türk's serve as examples, in which the lesions were a disseminated tuberculosis of the organs, as well as of the serous membranes; and, for instance, a second case reported by Diemer, in which obliterative pericarditis and atrophic cirrhosis of the liver occurred, but in which there was no note of ascites. I have been obliged reluctantly to omit also a number of cases reported by Italians —Galvagni, Bozzolo, Patella, and Caporali. Their reports were unavailable in the original, and the abstracts at my disposal were not sufficiently complete to enable me to incorporate them in the table.

Reporter.	Sex and age.	Duration, years.	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Van Deen, 1846	M. 40	2	Constant.	Subsequent to ascites.	Markedly thickened and firmly adherent to the heart.	Adherent throughout	Adherent throughout	Thickened throughout; many adhesions.	Chronic perihepatitis; liver otherwise normal.	Chronic perisplenitis; spleen otherwise normal.	The peritoneum of the under surface of the diaphragm and of the upper portion of the abdomen was least affected; pericarditis believed to be the primary affection, the pleuræ and the peritoneum being affected secondarily, the peritoneum through spreading of the inflammation through the diaphragm.
Frerichs, 1861	F. 38	2	Constant.	Constant, but moderate.	Firmly adherent throughout.	Adherent throughout	Adherent throughout	Cloudy, injected, and much thickened in many places.	Marked chronic perihepatitis; cirrhosis; liver one-third smaller than normal.	Marked chronic perisplenitis; spleen enlarged.	It is believed that the liver induration was caused by a peritonitis, the symptoms of which preceded by two years symptoms referable to the liver.
Feierabend, 1866	M. 50	4	Constant.	No.	Adher'nt and markedly calcified, especially the anterior surface; the apex free.	.....	.....	.....	Marked cirrhosis.	Enlarged.	Pericarditis 23 years previously; four tappings for relief of the ascites; the clinical diagnosis was cirrhosis of the liver with secondary gastro-intestinal catarrh.
Hambursin, 1869	M. 50	4	Constant.	Only shortly before death.	Chronic adhesions to the right of the base of the heart and to diaphragm; also fluid.	Chronic adhesions.	Normal.	Chronic adhesions and thickening.	Marked chronic perihepatitis; liver small, nutmeg, and cirrhotic.	Normal.	The disease is presumed to have begun in the liver capsule and to have implicated the pericardium subsequently.
Weiss, 1876	F. 51	1½	Constant.	Constant; moderate.	Thickened and adherent throughout.	Obliterated	Obliterated	Thickened & opaque; many adhesions.	Chronic perihepatitis; liver large and firm.	Chronic perisplenitis.	Presumed to have followed rheumatism; the anatomical diagnosis was total concretion of the abdominal and thoracic organs.
Weiss, 1876	F. 14	2	Constant	Only shortly before death.	Obliterated.	Fluid.	Obliterated	Thickened & opaque; many adhesions.	Chronic perihepatitis; liver firm.	Chronic perisplenitis.	Followed typhoid fever; many tappings for relief of the ascites.
Vierordt, 1884	F. 20	6	Constant.	Slight late in the course of the disease.	Obliterated.	Chronic adhesions.	Normal.	Thickened & opaque; many adhesions	Chronic perihepatitis; cirrhosis.	Chronic perisplenitis; spleen enlarged.	Presumed to have begun in the liver capsule: standstill for 1 year; 34 tappings (460 litres of fluid) for relief of the ascites.

Vierordt, 1884	F. 35	6	Constant.	Slight and transient.	Obliterated; marked calcification.	Obliterat'd; thickened.	Obliterat'd; thickened	Thickened & opaque; many adhesions.	Marked chronic perihepatitis (zuckergussleber); liver nutmeg.	Marked chronic perisplenitis (zuckergussmilz); spleen enlarged.	Presumed to have started in the pericardium; standstill for several years; several tappings for relief of the ascites; it is suggested that the peritonitis and the chronic inflammatory changes in the pericardium stand in some relationship to each other.
Curschmann, 1884	F. 54	6½	Constant.	No.	Obliterated; thickened.	Obliterat'd; thickened.	Acute serofibrinous inflammation.	Thickening, induration, opacity, and adhesions of the peritoneum of the upper half of the abdomen.	Diffuse chronic hyperplastic perihepatitis; compression and reduction in size (⅓) of the otherwise unaltered liver.	Marked chronic perisplenitis; spleen double the normal size.	Many tappings for relief of the ascites; standstill for a year and a half; recent tuberculous peritonitis at the necropsy.
Tissier, 1885	F. 51	10	Constant.	Yes.	Obliterated; calcification at left edge anteriorly & posteriorly; apex free.	Fluid.	Fluid.	Thickening, opacity and adhesions.	Marked chronic perihepatitis (zuckergussleber); liver enenlarged and nutmeg.	Chronic perisplenitis.	Several punctures for relief of the ascites.
Hirschler, 1886	F. 48	...	Constant.	Slight.	Obliterated.	Fluid.					
Weinberg, 1887	M. 19	½	Constant, though preceded by symptoms of acute pleuritis.	Subsequent to the ascites.	Thickened and obliterated.	Fluid.	Fluid.	Chronic peritonitis.	Chronic perihepatitis; liver nutmeg.	Enlarged.	Two tappings for relief of the ascites; process tuberculous, the result of primary infection of the pericardium by a tuberculous bronchial lymph gland.
Weinberg, 1887	F. 18	⅔	Constant.	Late in the course of the disease.	Thickened and obliterated.	Obliterated	Obliterated	Thickening, opacity and adhesions.	Chronic perihepatitis (not so marked on diaphragmatic surface as elsewhere); liver congested; weight 2050 grammes.	Normal.	Fifteen tappings for relief of the ascites; process tuberculous, the result of primary infection of the pericardium by tuberculous bronchial lymph gland.
Mott, 1887	M. 17	2½	Constant.	Only shortly before death.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Inflammatory lymph	Nutmeg; weight 54 ounces.	Normal.	Several tappings for relief of the ascites; process began as a pleuropericarditis.
Mott, 1887	M. 23	1½	Constant.	Subsequent to and less than the ascites.	Thickened and obliterated.	Recent serofibrinous exudate.	Thickened and obliterated.	.....	Enlarged; weight 5 pounds.	Congested; weight 18 oz.	Process began as a pleuropericarditis.

Reporter.	Sex and age.	Duration, years	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Variot, 1888	M. 51	...	Constant.	.....	Obliterated; marked calcification of anterior surface of right ventricle, left auricle, right edge, and posterior surface.	Chronic adhesions and fluid.	Chronic adhesions.	Chronic adhesions.	Marked chronic perihepatitis (zuckergussleber); liver enlarged.	Somewhat enlarged.	Clinical diagnosis: mitral insufficiency and right-sided pleural effusion.
Riedel, 1892	M. 19	15	Constant.	Only shortly before death.	Thickened and obliterated.	Chronic adhesions, thickening and fluid.	Chronic adhesions, thick'ning, and fluid.	Entire peritoneum markedly thickened and adherent.	Marked chronic perihepatitis (zuckergussleber) with extension of connective tissue into the liver substance.	Chronic perisplenitis; spleen enlarged.	Heart, lungs, liver, and spleen—zuckerguss; several tappings for relief of the ascites. Process presumed to have begun in the different serous membranes at the same time, although it is admitted that the disease may have begun in the pericardium as a complication of pertussis, and subsequently have implicated the other serous membranes by contiguity of structure. Standstill for eight years.
Cantu, 1894	F. 41	...	Constant.	.....	Thickened and obliterated.	Fluid.	Fluid.	.....	Nutmeg.	Congested.	
Rumpf, 1895	F. 49	16	Constant.	Of left leg.	Thickened and obliterated.	Chronic adhesions and fluid.	Chronic adhesions and thickening.	Thickening, opacity and adhesions.	Diffuse chronic hyperplastic perinephritis (zuckergussleber); compression of the otherwise unaltered liver.	Chronic perisplenitis; spleen moderately enlarged.	301 tappings for relief of the ascites; process presumed to have begun in the pericardium; acute pericarditis at the age of 33 years.
Henoch, 1895	M. 5	14 days (?)	Constant.	Constant.	Thickened and obliterated.	Thickened and adherent.	Thickened and adherent.	.....	Chronic perihepatitis; liver enlarged and cirrhotic.	Enlarged.	Presumed to be syphilitic.
Harris, 1895	M. 8	3½	Constant.	Slight.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Thickening, opacity and adhesions.	Marked chronic perihepatitis; liver nutmeg; little or no cirrhosis.	Marked chronic perisplenitis; spleen congested.	Many tappings for relief of the ascites; old tuberculous focus in the apex of the right lung; tuberculous arthritis of the right elbow.
Broadbent, 1895	F. 16	½	Constant.	Present, but much less than the ascites.	Thickened and obliterated.	.....	.....	Recent miliary tuberculosis.	Enlarged and nutmeg.	.....	Tuberculous focus in the apex of the left lung; striking feature of the case "the constant accumulation of fluid in the peritoneal cavity."

Pick, 1896	M. 47	4	Constant.	Slight.	Thickened and obliterated.	Fluid.	Chronic adhesions.	General fibrous peritonitis.	Chronic perihepatitis; liver enlarged and nutmeg.	Chronic perisplenitis; spleen congested.	Many tappings for relief of the ascites.
Pick, 1896	M. 26	8	Constant.	Late in the course of the disease.	Thickened and obliterated; extensive calcification.	Fluid.	Fluid.	.....	Enlarged and cirrhotic.	Enlarged five times the normal size.	Many tappings for relief of the ascites.
Pick, 1896	M. 24	2	Constant.	Subsequent to the ascites.	Obliterated; extensive calcification.	Chronic adhesions.	Chronic adhesions.	Thickening, opacity and adhesions.	Perihepatitis and cirrhosis.	Perisplenitis.	Process tuberculous; correct diagnosis during life.
Osler, 1896	F. 14	3½	Constant.	General at first; disappeared; reappeared; but always slight.	Thickened and partly obliterated.	Chronic adhesions.	.....	Thickening, opacity and adhesions.	Marked chronic perihepatitis and cirrhosis.	Perisplenitis; spleen enlarged and congested.	Correct diagnosis during life; extreme cyanosis of the hands and feet, and subcutaneous nodules about the knuckles, wrists, and elbows; 121 tappings for relief of the ascites.
Dickinson, 1896	F. 17	5	Constant.	Much less than the ascites.	Thickened and obliterated.	Chronic adhesions.	Obliterated	.....	Enlarged (64 oz.) and nutmeg; capsule thickened.	.....	26 tappings for relief of the ascites.
Heidemann, 1897	F. 15	1	Constant.	Subsequent to the ascites.	Obliterated.	Chronic adhesions and fluid.	Serofibrinous exudate.	Fibrous peritonitis, especially of Douglas' cul-de sac.	Small nutmeg and cirrhotic.	Somewhat enlarged.	Pericarditis one year previously; 23 tappings for relief of the ascites.
Schupfer, 1897	M. 44	4¾	Constant.	Slight at beginning; disappear'd and recurred shortly before death.	Obliterated.	Thickened and obliterated.	Thickened and obliterated.	Chronic fibrous hyperplastic peritonitis.	Marked chronic perihepatitis with extension of the connective tissue into the liver substance.	Perisplenitis.	Presumed to have begun at the same time in the different serous membranes; standstill for one year.
Cabot, 1898	M. 18	6	Constant.	Slight at intervals.	Obliterated.	Chronic adhesions and fluid.	Chronic adhesions and fluid.	.....	Enlarged and nutmeg.	.....	Several tappings for relief of the ascites.
Siegert, 1898	M. 19	9	Constant.	General at the beginning; disappeared, and recurred for short periods, & again before death.	Thickened and obliterated.	Chronic adhesions.	Chronic adhesions.	Thickening, opacity and adhesions.	Chronic perihepatitis with extension of connective tissue into the liver substance; liver congested.	Perisplenitis; spleen slightly enlarged.	Presumed to have begun in the pericardium; standstill for two and a half years; more than 100 tappings for relief of ascites.
Werbatus, 1898	M. 42	6	Constant.	Subsequent to the ascites.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Thickening, opacity and adhesions.	Chronic perihepatitis; atrophic nutmeg liver and cirrhosis.	Chronic perisplenitis and congestion.	

Reporter.	Sex and age.	Duration, years.	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Nachod, 1898	M. 6	1	Constant.	Slight at beginning; disappear'd and reappeared shortly before death.	Thickened and obliterated.	Extensive adhesions.	Extensive adhesions.	Chronic adhesions.	Liver firmer than normal; many caseous nodules in the capsule.	Enlarged; capsule thickened and contained many caseous nodules.	Nine months prior to death, with the idea that the ascites was due to tuberculous peritonitis, cœliotomy was performed, but the peritoneum was found entirely normal; the pericarditis evidently was primary; some bronchial glands were tuberculous.
Taylor, 1898	F. 42	1½	Constant.	Subsequent to the ascites.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Univers'lly thick and opaque.	Perihepatitis and compression of the liver.	Perisplenitis; spleen hard and small.	
Ewart, 1899	F. 49	4	Constant.	Slight.	Obliterated and calcified.	.....	.....	Adhesions and thickening.	Enlarged and congested.	Perisplenitis.	Operated upon for the cure of a supposed cirrhosis of the liver; previously to the operation fifty-two tappings for the relief of the ascites.
Diemer, 1899	M. 38	1½	Constant.	Present at first; disappeared, and reappeared.	Obliterated; extensive calcification, wide calcareous circlet about both ventricles; apex free.	Thickening and chronic adhesions.	Normal.	Diffuse thickening and adhesions.	Chronic fibrous perihepatitis (zuckergussleber); diffuse syphilitic cirrhosis.	Chronic perisplenitis (zuckergussmilz); chronic congestion.	Many tappings for relief of the ascites.
Schmaltz and Weber, 1899	F. 42	5	Constant.	Slight subsequent to the ascites.	Obliterated by recent adhesions.	Slight adhesions.	Adhesions.	Chronic adhesions.	Marked chronic perihepatitis (zuckergussleber); no connective tissue increase or marked congestion.	Marked chronic perisplenitis (zuckergussmilz); congestion.	Many tappings for relief of the ascites; standstill for two years.
Herrick, 1902	M. 20	4	Constant.	Present at first; disappeared and recurred.	Obliterated; extensive calcification of left half anteriorly & posteriorly, and of diaphragmatic surface.	Obliterated and thickened; small tuberculous sac.	Obliterated and thickened.	Smooth except for the perihepatitis and perisplenitis.	Chronic perihepatitis; liver firm; weight 2235 grammes; microscopic examination showed "cardiac cirrhosis."	Perisplenitis; spleen greatly enlarged.	Process tuberculous; several tappings for relief of the ascites and the pleural effusion; standstill for one year.
Kelly, 1902	M. 31	7	Constant.	Slight and transitory.	Obliterated; extensive calcification of both ventricles.	Thickened and obliterated.	Thickened and obliterated.	Recent hemorrhagic peritonitis	Chronic perihepatitis; congestion.	Congestion.	Several tappings for relief of the ascites.

Of the 39 cases in the table, 21 occurred in males, and 18 in females. The ages of the patients were as follows: 3 were under ten years of age; 13 were between eleven and twenty years; 3 were between twenty-one and thirty years; 5 were between thirty-one and forty years; 11 were between forty-one and fifty years; and 4 were between fifty-one and fifty-four years. This summary well illustrates a fact commented upon by a number of writers, namely, the prevalence of the disease among young subjects. Presumably, it indicates also that should the patient survive the twentieth year he or she is likely to live until the fourth decade of life. In 3 of the cases the duration of the disease was not ascertainable. In 26 cases the duration was two years or more; in 19 cases it was four years or more; in 1 case it was ten years; in 1 case it was fifteen years; and in 1 case it was sixteen years. In 1 case (Henoch's) the duration is put questionably at fourteen days. The striking clinical feature of all of the cases was the constant and predominating ascites, an ascites that necessitated many tappings and continuously recurred—whence the diagnosis in many cases of cirrhosis of the liver, in other cases of peritoneal tuberculosis. In most of the cases œdema of the legs was absent until shortly before death. In a few cases œdema was slight throughout the course of the disease, and in several of these it increased moderately or considerably shortly before death. In other cases it was present early in the course of the disease, but it soon disappeared, although the ascites persisted, and it did not recur until shortly before death; or it reappeared and disappeared irregularly throughout the course of the disease.

With regard to the anatomical lesions—in one case (Schmaltz and Weber's) the pericardium was obliterated by recent adhesions. In the remaining 38 cases the pericardium was thickened and obliterated by chronic adhesions—in almost all of the cases entirely obliterated, in one or two cases only partly obliterated. In 10 of the cases there was, in addition, more or less extensive calcification of the pericardium —the case herewith reported being the most marked example of this condition that I have encountered.

There is no statement with regard to the condition of the right pleura in 3 cases. In 1 case the right pleura contained recent serofibrinous exudate, in 6 cases it contained fluid, in 12 cases there were more or less extensive chronic adhesions, and in the remaining 17 cases the pleura was entirely obliterated and generally thickened. There is no statement with regard to the condition of the left pleura in 5 cases. In 3 cases the left pleura was normal, in 2 cases it contained recent serofibrinous exudate, in 4 cases it contained fluid, in 10 cases there were more or less extensive chronic adhesions, and in the remaining 15 cases the pleura was entirely obliterated and generally thickened. In most of the cases in which there were chronic adhesions fluid also was

present, and in most of the cases in which there were thickening and obliteration of the pleura and pericardial sacs there were also external adhesions binding the pericardium to the chest wall and external surface of the pleura and the adjacent tissues of the mediastinum. The summary well illustrates the more marked involvement of the right pleura as contrasted with the left pleura—a subject that has been much commented upon recently. There is no statement with regard to the condition of the general peritoneum in 8 cases. In 1 case there was recent hemorrhagic peritonitis, in 1 case recent miliary tuberculosis, and in 1 case inflammatory lymph, and in the remaining 28 cases there were more or less extensive chronic adhesions.

There is no statement with regard to the condition of the liver in 1 case. In 28 cases chronic perihepatitis was noted, and in 31 cases there was either chronic perihepatitis or chronic peritonitis or both. The liver itself was reported to be nutmeg in appearance in 14 cases, cirrhotic in 8 cases, large and firm in 5 cases, normal aside from compression in 4 cases, nutmeg and cirrhotic in 4 cases, and in 3 cases there appeared to be only extension of connective tissue from the thickened capsule into the substance of the organ. Perisplenitis was noted in 23 cases. There was no statement with regard to the condition of the spleen itself in 12 cases. In 23 cases it was congested, in 1 case it was small and hard, and in 3 cases it was normal.

From this tabulation and summary two facts stand out prominently: 1. That although all the cases presented ascites as the striking clinical feature and revealed obliterative pericarditis at the necropsy, yet that organ that we might presume to be most at fault—the liver—presented a variety of lesions in the different cases; and 2, that in all the cases more than one serous membrane, in some of the cases all the serous membranes were diseased. The feature possessed by the cases in common, therefore, is widespread disease of the serous membranes, and the most common lesion is chronic hyperplastic serositis.

In some cases there is a clear history of the repeated occurrence of inflammation of one or more serous membranes; in other cases the disease was latent and entirely unsuspected during life. In some cases the history points definitely to a certain serous membrane as the point of departure of the disease, to the membrane whence the inflammatory process spread to the other membranes. In this connection, however, we should bear in mind that the serous membrane disease that attracted attention in some of these cases began acutely, and that such disease of a serous membrane may just as well be the consequence as the cause of a latent inflammation of some other serous membrane. Thus it is that in some of the cases with multiple involvement of the serous membranes, different writers interpret the necropsy findings differently. Some attribute the symptom complex to a primary pericarditis with consecu-

tive pleuritis and peritonitis; others hold the opposite view, and look upon the peritonitis as the primary event, and attribute the pleuritis and pericarditis to extension of the inflammation through the diaphragm from a perihepatitis; others hold that the perihepatitis is the primary disease and that from this by continuity and contiguity of structure the peritonitis and the pericarditis arise; and, finally, still others hold that all of the serous membranes become infected with the same noxious agent at the same time.

From this point of view Picchini distinguishes four groups of cases of multiple serositis or polyserositis: 1. Cases in which by means of careful inquiry the point of origin of the disease, that is, the serous membrane first affected, as well as the order of the involvement of the other serous membranes, may be determined. 2. Cases in which on inquiry the point of origin of the disease may be determined, but in which the first examination of the patient reveals that several serous membranes are already affected, although they manifest no clinical symptoms. 3. Cases in which the history reveals that from the beginning several serous membranes have been affected. 4. Cases in which from the history it cannot be determined whether the disease began with inflammation of one or more serous membranes. Of the 50 cases observed by Picchini, 37 belonged to the first group; 11 to the second; 1 to the third, and 1 to the fourth group. Of 110 collected by Picchini (50 observed by himself and 60 collected from the literature) the peritoneum was involved in all, although this was recognized clinically in only 13 of the cases. This peritonitis was not only the most frequent, but also the most important lesion; it dominated the situation. Pleuritis was present in 109 cases, in 73 of which it was bilateral. The pericardium was least frequently involved—only in 9 of 50 cases. This fact is deemed evidence of great resistance on the part of the pericardium.

De Renzi states that in multiple serositis the peritoneum is usually involved first; then the right pleura, and then the pericardium. If, however, the right pleura should be involved first, the disease then extends to the peritoneum, thence to the left pleura and the pericardium. In some cases, however, this mode of progression of the disease is not preserved, as sometimes a pericarditis that usually is not to be diagnosticated develops first. De Renzi states further that the disease is characterized by the fact that it remains localized to the serous membranes; that it does not implicate the intra-abdominal and intrathoracic organs; that it pursues a remarkably slow and insidious course; that it gives rise to the exudation of large quantities of serofibrinous fluid; and that the fluid portion of the exudate tends to become absorbed, in consequence of which fibrous adhesions with complete obliteration of the serous cavities result.

Presuming, then, that the inflammation may begin in any serous membrane, it is evident that the clinical manifestations may vary, depending upon the serous membrane first affected. This is commented upon by a number of writers, and it is discussed at length by Siegert, who points out that although the chronic perihepatitis and the resultant ascites dominate the clinical picture, the clinical picture nevertheless assumes quite different aspects depending upon whether the disease begins in one or more serous membranes. Thus, if the liver capsule is first affected ascites occurs as an inflammatory exudate. If after the lapse of some time the perihepatitis leads to compression of the liver and the portal radicles, another factor contributing to congestion and ascites is added. Thus it is that ascites is the prominent symptom in those cases of multiple serositis in which the disease begins in the peritoneum. Later in the course of the disease the marked increase in the intra-abdominal pressure occasioned by the large amount of the ascites, as well as the spread of the inflammatory process to the pleura and the pericardium, may lead to congestion in the area of collection of the inferior vena cava, so that to the ascites œdema of the legs is added.

That multiple serositis may begin in one or the other pleura must be conceded, and that such is really the case is rendered likely by the history of early and apparently primary pleuritis in several of the cases tabulated. Especial interest, however, attaches to primary involvement of the pericardium. In the reports of some of the cases tabulated there appears a note that acute pericarditis occurred some years prior to the development of the symptoms that interest us at present, and in other of the cases the nature and the extent of pericardial lesions warrant the assumption that these were the primary lesions—for instance, the cases reported by Feierabend, Vierordt, Weinberg, Mott, Riedel (?), Rumpf, Pick, Osler, Heidemann, Siegert, Nachod, Ewart, and my own case. When the pericardium is primarily affected certain features in the clinical course of the disease may occur that possess especial interest and diagnostic importance. Whereas in those cases in which the peritonitis or perihepatitis is the primary event, ascites occurs early and is succeeded by œdema only late in the course of the disease, in the cases beginning with pericarditis œdema of the legs may occur early—the consequence of early and transitory insufficiency of the myocardium. In cases in which this occurs the œdema usually soon disappears and is succeeded by ascites, which assumes and maintains the ascendency—for instance, cases reported by Vierordt, Broadbent, Rumpf, Osler, Dickinson, Schupfer, Siegert, Nachod, and Diemer. However, as pointed out by Siegert, the absence of œdema of the legs in the presence of ascites early in the course of the disease is no evidence of primary implication of the peritoneum rather than of the pericardium, since

it is well known that chronic obliterative pericarditis frequently runs a course entirely devoid of symptoms.

The cause of this obliterative pericarditis, as well as the cause of the multiple serositis in general, has occasioned considerable discussion. Certain of the infective diseases, such as typhoid fever, pertussis, malaria, syphilis, and rheumatism, are given as etiological factors in a number of the cases tabulated. In a number of the cases the lesions are of extremely obscure or unknown etiology, whereas, in other cases the provoking agent was certainly the tubercle bacillus. The fact that possesses considerable interest in this connection is that during recent years medical writers have become more and more inclined to look upon many cases of chronic obliterative pericarditis (as well as disease of other serous membranes) as tuberculous in nature, and this even in the absence of clear evidence of tuberculosis. This has been insisted upon for a number of years by the German and the Italian writers, and it is emphasized by Riesman and by Wells in their recent communications. According to a number of writers the disease is always tuberculous in nature; other writers, however, are disposed to admit the occasional operation of other etiological factors, inasmuch as it has not been possible to demonstrate the tuberculous nature of all cases by either macroscopic, microscopic, or bacteriologic examinations. The important fact to bear in mind is that many cases apparently non-tuberculous are in reality due to the tubercle bacillus, and that in some cases characteristic tuberculous lesions may be detected by microscopic examination of the tissues, and that the tubercle bacillus may be recovered from some of the lesions by appropriate bacteriologic and inoculation procedures. Presumably, also, the patient would react to tuberculin injections. On the other hand, that a number of cases are not tuberculous must be conceded. In my own case careful microscopic examination of the tissues failed to disclose any tuberculous lesions. I would suggest that in my own case, as well as in other cases, antecedent rheumatism possesses considerable etiological importance. In some cases chronic nephritis may be the etiological factor; whereas in other cases the disease seems to develop from cholelithiasis with cholecystitis and pericholecystitis (localized peritonitis).

An important and interesting fact especially insisted upon by the Italian writers is that not every case of general tuberculosis that implicates the serous membranes and gives rise to chronic fibrous lesions belongs to the group of cases under discussion. Picchini states that the cases under discussion differ from the ordinary cases of serous membrane tuberculosis in that in their etiology heredity appears to play no rôle; that the disease does not appear to affect especially persons of phthisical or tuberculous habitus; that the inflammations of the serous membranes set in insidiously, much less acutely than do the

ordinary cases of tuberculous inflammation; that they may remain latent for a long time; and that the lesions remain localized to the serous investment of the organs and are unassociated with tuberculous lesions of the lungs, as is so common in the ordinary cases. A study of the cases reported in the literature bears out the reasonableness of this view.

A marked susceptibility of the serous membranes and a certain immunity of the organs to the cause of the disease—presumably the tubercle bacillus in many of the cases—appear to be striking features of the cases. Nevertheless, there seem to be border-line cases and cases representing varying degrees of infection with the tubercle bacillus: 1. Cases in which the lesions are confined strictly to the serous membranes. 2. Cases in which the lesions involve, especially the serous membranes, but in which one or several tuberculous foci may be found in the body—for instance, the cases reported by Weinberg, Harris, Broadbent, Pick, and Nachod. 3. Cases in which the serous membrane disease represents but a part of a general tuberculous infection (not considered in this communication). That this is probably true is borne out by the fact that in one or two of the cases the fatal termination was brought about by an acute disseminated miliary tuberculosis. Cantu accounts for the peculiarities of the disease as contrasted with the ordinary cases of tuberculosis of the serous membranes by assuming that it is due to a special form of the tubercle bacillus. On account of the length and arrangement of the tubercle bacilli in the newly formed connective tissue in his case, he assumed that the bacillus operative was allied to that form peculiar to birds.

Some discussion has been occasioned by certain writers—Pick, Schupfer, Werbatus, Heidemann, and others—including the group of cases under consideration, the cases of "zuckergussleber," reported by Curschmann, Rumpf, and Hübler. Reference to the table will show that the cases of Curschmann and of Rumpf are in reality cases of multiple serositis, that in them the lesions of the serous membranes were widespread. In Hübler's case, as well as in a number of cases reported by Hale White, the lesions were confined to the peritoneum. Inasmuch, however, as the lesions in these cases are similar to the more widespread lesions in the other cases, it is warrantable to group all of them in the same category as cases of more or less extensive serositis. The cases differ among themselves in the extent and intensity of the serous membrane involvement, but in all the cases the lesions are alike. We have to explain, however, the greater intensity of the lesions about the liver in the cases in which the peritoneum is the only serous membrane involved, as well as in other cases in which the pleuræ and the pericardium also are involved.

The intensity of the lesions about the liver finds its explanation in

certain facts known regarding the anatomy, physiology, and pathology of the peritoneum and its circulation. The facts that interest us at present have been worked out by a number of investigators, and they have been confirmed and summarized by Clark about as follows: Fluids and solids may pass through the endothelial layer of the peritoneum, the fluids in many places, the solid particles only through the central tendon in the diaphragm. Minute particles are carried in an incredibly short time from the peritoneal cavity through the diaphragm into the mediastinal lymph vessels and glands, and thence into the blood circulation, by which they are distributed to the abdominal organs, to appear in the collecting lymph glands of these organs. The leucocytes are largely the bearers of foreign bodies from the peritoneal cavity through the diaphragm into the mediastinal lymph vessels and thence into the blood circulation. There is normally a force in the peritoneal cavity which carries the fluids and foreign particles toward the diaphragm, regardless of the posture of the patient, though gravity can greatly favor or retard the current. It is pointed out also by Clark that under normal circumstances the peritoneum can dispose of pyogenic organisms in varying number, depending upon the virulence of the organism, without producing peritonitis, and that the pathways whereby these are eliminated are as just mentioned, that is, toward the central tendon of the diaphragm and thence to the mediastinal lymph glands.

Now, what I believe is that what is true as regards experimental work and acute infections is true also as regards chronic infections; that is, the attempt on the part of the peritoneum to remove certain noxious agents—for instance, the tubercle bacillus, the infective agent of rheumatism and other diseases, probably certain toxic substances—may result in partial or complete success. In the latter instance the peritoneum may be completely rid of the infective agent, which, being carried to the mediastinal lymph vessels and lymph glands may infect the pericardium or the pleura, giving rise to a primary pleuritis or pericarditis. Subsequently the peritoneum may become infected. In other cases the attempt on the part of the peritoneum to remove the infective agent being only partially successful, the region about the liver and the under surface of the diaphragm succumbs, and a primary perihepatitis occurs. Subsequently the infective agent may travel through the diaphragm and infect the pericardium, or the pleura, or both. In these cases, on account of the peculiar lymphatic supply of the surface of the liver and the under surface of the diaphragm, the infective agent being as it were concentrated to the region about the liver, especially to the neighborhood of the suspensory ligament toward which many of the lymphatics converge, gives rise to the excessive and often hyperplastic lesions sometimes observed. The peculiarities of course and of distribution of the lymphatics of this region are also accountable

for the much greater involvement of the upper surface of the liver (as contrasted with the lower surface) that is present in most of the cases. In this class of cases the primary infection of the peritoneum may be hematogenic in origin; or it may be of more local source, such as the intestinal tract or the urinary organs; or, in the case of women, it may result from some genital infection, as appears to have been the fact in Caporali's case. In a number of cases, on the other hand, a primary pericarditis occurs independently of peritoneal infection. Many of these cases are tuberculous in nature—the result generally of extension of disease from tuberculous mediastinal or peribronchial lymph glands, a subject recently discussed at length by Riesman. Following such initial infection of the pericardium the other serous membranes may become implicated in the diseased process. Thus either an ascending or a descending infection of the several serous membranes may occur; and there is no reason for not believing that in some cases all the serous membranes may become infected at the same time by the same infective agent.

The condition of the liver in these cases now demands consideration. In assigning to the liver a rôle in the production of the ascites we have to bear in mind that in 31 of the cases tabulated chronic peritonitis or chronic perihepatitis or both were present. (There is no note with regard to the condition of the liver in 1 case.) Thus in 31 of the cases the ascites may be accounted for without reference to the condition of the liver substance. In the 7 cases in which there is no note of perihepatitis or peritonitis the liver is described as nutmeg or cirrhotic, or both. In the case of cirrhosis (Feierabend) the ascites may be attributed to the cirrhosis, which may have been an independent affection or the consequence of the long-standing congestion. With regard to the remaining 6 cases—1 of Mott's showed recent inflammatory lymph in the peritoneum, Broadbent's showed recent miliary tuberculosis, whereas the reports of the other 4 cases (Mott, Cantu, Pick, and Cabot) contain no statement whatever with regard to the condition of the peritoneum.

In the absence of statements to the contrary, assuming that the peritoneum was normal in these cases, the cases in which one has to invoke the activity of the liver alone to explain the occurrence of the ascites are still very few. In the majority of cases the ascites is satisfactorily explained by the perihepatitis and the peritonitis, and this fact has to be borne in mind by those that would assign predominance to the liver in the causation of the ascites.

Again, the condition of the liver in the majority of these cases is scarcely that which we usually associate with the production of ascites. In the cases in which the liver was normal aside from compression, as well as in the cases in which there appeared to be only extension of connective tissue from the thickened capsule into the substance of the

organ, predominance in the production of the ascites cannot be ascribed to the liver. Even with regard to the cases in which, in addition to the perihepatitis, cirrhosis of the liver was present, we have to bear in mind that the ascites, in most of the cases, was present at a time when clinically the liver was normal in size or enlarged and presumably not cirrhotic. With regard to the cases in which the liver was large and firm or nutmeg in appearance we have to bear in mind that most of the livers that were subjected to careful microscopic study revealed, as a rule, only varying degrees of chronic congestion and its consequences, and that in many cases the entire absence of periportal connective tissue proliferation has been emphasized. In some of the other cases the connective tissue proliferation although present has been inconspicuous—certainly in most of the cases insufficient alone to account for the ascites, a subject discussed in detail by Eisenmenger. Contrary to the opinion held by Pick and others, therefore, I believe that in the majority of cases primary importance in the production of the ascites cannot be assigned to the liver. However, that the condition of the liver may be a contributing factor in the causation of the ascites, and in the increase of an ascites produced by the serositis (perihepatitis or peritonitis), as for instance, in cases of associated cirrhosis, etc., must be conceded; that in a few cases the ascites may be brought about in the manner maintained by Pick, that is, as a direct result of the congestion of the liver, may also be conceded. These, which are rare cases, may be likened to the unusual cases of valvular disease of the heart in which disproportionate ascites occurs. Still, it is important to bear in mind that these two classes of cases differ in this respect—that an isolated ascites, such as was present for a long time in many of the cases herewith tabulated, rarely if ever occurs in valvular disease of the heart. In both disproportionate ascites is not uncommon; in valvular disease of the heart, however, the disproportionate ascites is accompanied by more or less œdema of the extremities, as well as of the trunk—an association that is not uncommon in certain cases of obliterative pericarditis. Under such circumstances the differential diagnosis between these two conditions is a matter of extreme difficulty, if not of impossibility — a subject recently discussed in detail by Türk.

At present, however, I am concerned not so much with this class of cases as with that class in which for a long time isolated ascites is the striking clinical feature. I am inclined to concur with Rosenbach, who states that in these cases the ascites must be the result of the operation of special conditions which although associated with the heart (or pericardial) disease are not the direct result of diminution of the power of the heart and of consequent congestion. While it is probable that all the cases that present the complex of obliterative pericarditis and

ascites may not be of the same nature, I should like to emphasize the importance of the perihepatitis and the peritonitis in the causation of the ascites.

In this connection I cannot forbear to refer to some extremely interesting observations made some years ago by Hale White. This writer, basing his remarks upon 34 cases of cirrhosis of the liver, stated that he was not able to find the report of a single case of uncomplicated cirrhosis of the liver in which the patient long survived paracentesis of the abdomen, that not one patient lived long enough for paracentesis to become necessary a second time, and that many patients died before it became necessary at all. Referring then to a group of 10 cases that had been regarded as cases of cirrhosis of the liver but in which paracentesis had been performed more than once, he concluded: That the supervention of ascites in uncomplicated cirrhosis of the liver means that the end is near; that if a patient with ascites and cirrhosis of the liver lives long enough to require a second paracentesis, it is in the highest degree probable that either the diagnosis is incorrect or that some cause other than cirrhosis exists to explain the ascites; and that such cases nearly always turn out to be examples of chronic peritonitis, with perihepatitis, which is not a special disease but merely a part of chronic peritonitis. I cite these observations merely to emphasize the relative unimportance of the liver in the causation of an ascites that persists as long as, and necessitates as many tappings as, does the ascites in the cases at present under discussion. That recurring ascites occurs in the absence of congestive alterations in the liver is well illustrated also by the case reported by Hübler. In this case, as well as in a number of cases reported by Hale White and others, the serous membrane disease was confined to the peritoneum. Clinically these cases were the counterpart of many of the cases herewith tabulated, but at the necropsy the pleuræ and the pericardium were found intact. There was absence of congestive alterations in the liver, absence of connective tissue hyperplasia in the liver, but there were marked hyperplastic perihepatitis (zuckergussleber) and recurring ascites.

To RECAPITULATE: In a certain proportion of cases of chronic obliterative pericarditis ascites is the striking clinical symptom, and leads usually to the diagnosis of cirrhosis of the liver—whence the somewhat unhappy designation "pericarditic pseudocirrhosis of the liver," suggested by Pick, is not altogether inappropriate. Anatomically the distinguishing feature of these cases is a chronic fibrous (usually hyperplastic) inflammation of the several serous membranes of the body—a multiple serositis. In some cases the inflammation may remain localized to one or two serous membranes, but there exists a marked tendency for all the serous membranes to become involved. The several serous membranes may become involved equally or unequally; usually the

lesions are most marked in the pericardium and on both sides of the diaphragm. In some cases extensive calcification of the pericardium occurs—the case herewith reported being the most marked example of this condition that I have ever encountered. In cases in which there is but partial obliteration of the pleural or the pericardial sacs there is usually also some fluid present. In many cases, however, not only is the pericardium thickened and obliterated, but it has also formed adhesions with the chest wall and the structures of the mediastinum, one or both pleuræ are thickened and obliterated, and the peritoneum is more or less thickened and adherent and contains a large quantity of fluid. In many cases the liver is adherent not only to the under surface of the diaphragm, but also to the stomach, the colon, the omentum, the anterior abdominal wall, etc. The lesions involve also the spleen, especially in those cases in which there are extensive adhesions in the left pleura. A distinguishing feature of the lesions is the development of thick fibrous, almost cartilaginous masses of connective tissue, that encase, compress, and often distort the organs, and give rise to an appearance suggesting confectioners' icing—whence the designation "iced liver" (zuckergussleber). In many cases of primary pericarditis the liver is enlarged, smooth, and has sharp edges; later with the development of the perihepatitis, the liver lessens in size, its surface becomes somewhat irregular, its edges rounded, and sometimes the entire organ becomes much distorted; still later or in some cases earlier the appearances characterized as nutmeg, with or without atrophic alterations, may supervene. Although some slight connective tissue proliferation and some extension of newly formed connective tissue from the thickened capsule sometimes occur, the common absence of marked connective tissue proliferation in the liver is noteworthy. In some cases the lesions of cirrhosis are encountered.

As already stated, the striking clinical feature of the disease is ascites, which is present whether the pericardial and pleural changes are absent, whether they are slight, or whether they are marked. However, the interpretation of the phenomena of the disease is much facilitated by recognizing that taken as a whole—from the beginning to the end—the symptom complex is made up of symptoms due to the serositis and of symptoms due to the disturbances or failure of the circulation induced by the pericardial part of the serositis. As a matter of fact, aside from the ascites, which occurs early, and may be the only symptom for many years, the symptoms are due almost entirely, if not entirely, to failing cardiac compensation. Expressing my own opinion, I should say that there can be little doubt that presenting the complex of obliterative pericarditis and ascites, there are grouped a number of cases that differ more or less in nature the one from the other. However, I believe that

in the majority of cases the ascites is due primarily to the peritonitis and the perihepatitis; that in consequence of the inflammation, the peritoneum becomes a locus minoris resistentiæ; that in consequence of the chronic pericarditis—in reality the pancarditis—the functional activity of the myocardium is interfered with; that in consequence of the lessening of the functional activity of the myocardium the circulation of the blood is more or less impeded—in some cases insensibly impeded; that the region that first manifests the sensible evidences of impeded circulation is the locus minoris resistentiæ—the peritoneum; that the relief afforded the general venous circulation by the accumulation of the ascites, probably indirectly, prevents to some extent the occurrence of œdema of the extremities; that the connective tissue hyperplasia of the liver in some of the cases is due to the same causes that induce the serous membrane inflammation—the irritant being carried by the lymphatics into the liver substance from the diseased capsule; and that in different cases the ascites is increased by the contraction of the newly formed connective tissue of the capsule, by the concomitant peritonitis in the transverse fissure of the liver should it compress the vessels (which occurs rarely if at all), by the marked congestion and its consequences, by concurrent cirrhosis (which is unusual), and by the general failure of the circulation toward the close of life.

Thus, although the disease is characterized by slow, insidious, and intermittent course, the perihepatitis and the peritonitis dominate the clinical picture of the well-developed disease. Aside from this, that is, aside from the ascites, the clinical picture varies, depending upon the point of origin of the disease. In some cases the disease is ushered in with acute pericarditis, pleuritis (which may necessitate repeated tappings), or perihepatitis (circumscribed peritonitis), which subsides and leaves the patient apparently well for a number of years. Usually, however, the lesions of the pericardium and of the pleuræ are latent, and the first sensible evidence of the disease is ascites. In some cases of primary pericarditis slight and transient œdema of the legs may be present clearly, but this is not observed in many cases, inasmuch as the pericarditis is usually latent. When œdema does occur early it usually soon subsides and does not recur until the ascites has been present for a long time or until shortly before death. Except shortly before death it is inconspicuous when contrasted with the excessive ascites. (Reference is not made in this communication to that class of cases in which general failure of the circulation occurs early and in which œdema and ascites develop pari passu.) Associated with early œdema, slight swelling of the spleen and disturbances of the gastro-intestinal tract may develop, but these usually subside with the ascites, and the disease, as a rule, is characterized by the entire absence of such symptoms until

shortly before death. The ascites is characterized by the fact that it is excessive, that it necessitates repeated tappings, that it recurs rapidly after tapping, and that it may remain stationary (not necessitating tapping) for many years.

In a few cases lesions of the peritoneum appear to be entirely absent, whereas, in other cases they are so slight as to appear inadequate to cause the ascites. These cases may be likened to the similar cases of valvular disease of the heart in which disproportionate ascites is the striking clinical feature. In these cases the ascites is doubtless due directly to the congestion of the liver and its consequences, as maintained by Pick. In some cases both factors—the congestion of the liver and the peritonitis—are operative; in some cases rather the congestion of the liver, in other cases rather the peritonitis. In cases in which the congestion is the major factor we should expect more or less swelling of the spleen and disturbances of the gastro-intestinal tract; in cases in which the serositis is the major factor, we should expect an absence of such symptoms. Some distinction—anatomically, at least—may be drawn between cases in which the lesions are confined to the peritoneum and cases in which the lesions are more wide-spread. The cases in which the pericardium is unaffected reveal no congestive alterations in the liver. Clinically, however, the two classes of cases are very much alike, and the "zuckergussleber" may occur in both.

In the diagnosis of this multiple serositis or of chronic adhesive pericarditis with ascites, especial attention should be directed to the history of a previous attack of acute pericarditis, pleuritis, or perihepatitis; to the early occurrence and subsequent disappearance of the œdema of the legs; to the marked ascites, with little or no œdema of the legs; to the enlarged liver early in the course of the disease (in some cases the liver appears not to have been enlarged), and to the small and distorted, but otherwise smooth liver, in the later stages of the disease; to the absence or very late occurrence of marked enlargement of the spleen; to the tendency to the occurrence of repeated attacks of pain, tenderness, rigidity, and possibly palpable and audible frictions in the right hypochondriac region—attributable to attacks of perihepatitis; to the rapid recurrence of the ascites after tapping, and to the physical signs of adherent pericardium—without which, it may be said, the disease is incapable of diagnosis. In the diagnosis of adherent pericardium most help will be derived from: a weak or absent apex-beat, especially in cases in which there is no increase in the area of cardiac dulness; systolic retraction of a considerable area about the apex; systolic retraction of the base of the left chest posteriorly; arrest of the normal respiratory movements in the epigastric angle; imperfect descent of the apex-beat during inspiration; inadequate or entire absence of

shifting of the apex-beat, with change in the posture (lateral posture) of the patient; absence of change in the limits of the cardiac dulness during the respiratory phases; absence of increase of the cardiac dulness to the right, despite marked engorgement of the veins of the neck; a diastolic shock or rebound of the heart; evidences of dilatation or hypertrophy of the heart in the absence of valvular or other disease that might cause it; absence of the characteristic changes in the heart in the presence of definite valvular disease—that is, absence of the usual hypertrophy of the right ventricle in mitral disease and of the left ventricle in aortic disease; absence of pericardial effusion in the presence of pleural and peritoneal effusions; paradoxic pulse—inspiratory diminution in the force and volume of the pulse; diastolic collapse and inspiratory swelling of the veins of the neck; and, as suggested by Musser, the non-occurrence in young subjects with valvular disease and cardiac insufficiency of the characteristic improvement following the administration of digitalis. None of these is pathognomonic of adherent pericardium; all will not be present in every case; but in many cases a sufficient number may be present to warrant the diagnosis.

Finally, this obliterative pericarditis with ascites may be distinguished from cirrhosis of the liver: by the aforementioned symptoms and signs of adherent pericardium; by the absence of the etiological factors of cirrhosis of the liver; by the slow, insidious, protracted, and intermittent course of the disease; by the long periods of standstill during which the ascites may remain stationary and the patient in good condition; by the entire absence or the transient presence of slight jaundice; by the absence in most cases of portal congestion and gastro-intestinal disturbances—hemorrhage, diarrhœa, hemorrhoids, enlargement of the spleen, marked dilatation of the superficial veins of the abdominal wall, etc.; in some cases, by the association of an enlarged, smooth, and firm liver, with marked ascites; and by the fact that in many cases the patient survives a large number of tappings.

References.

Bamberger. Krankheiten des chylopoetischen Systems. Virchow's Handbuch der speciellen Pathologie und Therapie, 1864, 2te Aufl., vol vi. p. 495

Bozzolo. Pericardite latente; pseudocirrhose del fegato. Clinica moderna, 1898, No. 8; Centralblatt für innere medicin, 1899, vol. xx. p. 733.

Broadbent. Adherent Pericardium, 1895. British Medical Journal, 1898, vol. i. p. 147.

Cabot. Obliterative Pericarditis as a Cause of Hepatic Enlargement and Ascites. Boston Medical and Surgical Journal, 1898, vol. cxxxviii. p. 463.

Cantu. Cited by Hager, loc. cit.

Caporali. Cirrose capsulare del fegato da peritonite cronica. Riforma Medica, 1898, vol. xiv. pp. 149, 160; Centralblatt für innere Medicin, 1899, vol. xx. p. 394.

Clark. Elimination of Peritoneal Infection and Prevention of Surgical Peritonitis. Journa of the American Medical Association, 1901, vol. xxxvii. p. 360.

Curschmann. Zur Differential Diagnostik der mit Ascites verbundenen Erkrankungen der Leber und der Pfortadersystem. Deutsche medicinische Wochenschrift, 1884, vol. x. p. 564.

De Renzi. Cited by Hager, loc. cit.

Dickinson. Adherent Pericardium as a Cause of Fatal Enlargement of the Heart. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1896, vol. cxii. p 691.

Diemer. Ueber Kalkablagerungen an den serösen Hauten des Herzens. Zeitschrift für Heilkunde, 1899, vol. xx. p. 257.

Eisenmenger. Ueber die sogenannte pericarditishe Pseudolebercirrhose (Fr. Pick). Wiener klinische Wochenschrift, 1900, vol. xiii. p. 249.

Ewart. Calcification of the Adherent Pericardium. British Med. Journal, 1899, vol. i. p. 908.

Fagge. Observations on Some Points Connected with Diseases of the Liver or the Peritoneum. Guy's Hospital Reports, 1875, vol. xx. pp. 196, 202.

Feierabend. Verknocherung der vorderen Herzwand mit Lebercirrhose. Wiener medicinische Wochenschrift, 1866, vol. xvi. p. 924.

Frerichs. Klinik der Leberkrankheiten, 1861, vol. ii. p. 90. Die einfache chronische Exudativperitonitis, Tübingen, 1884, pp. 78, 117, 132.

Galvagni. Sulla pericardite callosa. Clinica moderna, 1898, vol. iv. pp. 257, 265; Centralblatt für innere Medicin, vol. xx. p. 733.

Girardeau. Des pericardites, Paris, 1893. British Medical Journal, 1900, vol. i. p. 1498.

Hager. Ueber Polyserositis. Festschrift zur Feier des 50 jährigen Bestehens der medicinischen Gesellschaft zu Magdeburg, 1898, p. 39.

Hambursin. Nouvelle observation de péricardite consécutive à une périhepatite. Bulletin de l'Academie de Médecine de Belgique, 1870, vol. iv. p. 990.

Harris. Indurative Mediastino-pericarditis. Medical Chronicle, 1895, vol. ii. pp. 1, 87, 178. 250.

Heidemann. Ueber die Folgezustande von pericardialen Obliteration. Berliner klinische Wochenschrift, 1897, vol. xxxiv. pp. 92, 119.

Henoch. Vorlesungen über Kinderkrankheiten, 9te Aufl., 1895, p. 442.

Herrick. Pericarditic Pseudocirrhosis of the Liver. Transactions of the Chicago Pathological Society, April, 1902.

Hirschler. Hochgradiger Ascites ohne entsprechendes Anasarca der unteren Extremitäten in einem Falle von Herzbeutelverwachsung. Pester med.-chir. Presse, 1886, No. 15; Centralblatt für innere Medicin, 1886, vol. vii. p. 722.

Hübler. Ein Fall von chronischer Perihepatitis hyperplastica. Berliner klinischer Wochenschrift, 1897, vol. xxxiv. p. 1118.

Hutinel. Symphyse du pericarde. Gazette hebdomadaire de Médecine et de Chirurgie, 1901, nouvelle serie, vol. vi. p. 61.

Leube. Specielle Diagnose innerer Krankheiten, 1891, vol. i. p. 48.

Liebermeister. Beiträge zur path. Anatomie und Klinik der Leberkrankheiten, 1864, p. 119.

Mott. Adherent Pericardium with Ascites and Anasarca. Practitioner, 1887, xxxviii. p. 95.

Murchison. Clinical Lecturers on Diseases of the Liver, 1868, pp. 240, 460.

Musser. Medical Diagnosis, fourth edition, 1900, p. 654.

Nachod. Zur Kenntniss der perikarditischen Pseudolebercirrhose (Pick). Prager medicinische Wochenschrift, 1898, vol. xxiii. p. 329.

Oppolzer. Chronische Leberatrophie. Wiener allgemeine med. Zeitung, 1866, vol. xi. p. 141.

Osler. Chronic Perihepatitis and Mediastino-pericarditis. Archives of Pediatrics, 1896, vol. xiii. p. 3; Practice of Medicine, second edition, 1895, p. 625.

Patella. Dell' ascite in casi di pericardite adesiva (pseudocirrose del fegato d'origine pericarditica, Pick). Clinica moderna, 1898, No. 2; Central. für innere Medicin, 1899, vol. xx. p. 732.

Picchini. Il Morgagni, 1901; cited by Hager, loc. cit.

Pick. Ueber chronischer, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose). Zeitschrift für klinische Medicin, 1896, vol. xxix. p. 385. Ueber perikarditische Pseudolebercirrhose. Verhandlungen des XVII. Kongresses für innere medicin gehalten zu Karlsbad, 1899, p. 588. Erwiderung auf Dr. Eisenmenger's Aufsatz: "Ueber die sognnante Pseudolebercirrhose" (Fr. Pick). Wiener klinische Wochenschrift, 1900, vol xiii. p. 324.

Quincke und Hoppe-Seyler. Die Krankheiten des Leber. Nothnagel's Specielle Pathologie und Therapie, 1899, vol. xviii. p. 283.

Riedel. Ein Fall von chronischer idiopthischer exudativer Peritonitis. Münchener medicinische Wochenschrift, 1892, vol. xxxix. p. 798.

Riesman. Primary Tuberculosis of the Pericardium. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1901, vol. cxxii. p. 6.

Roberts. Diseases of the Mediastinum and Thymus Gland. Allbutt's System of Medicine, 1900, vol. vi. p. 78.

Rokitansky. Handbuch der speciellen pathologischen Anatomie, 1842, vol. ii. pp. 317, 335.

Rose. Zur Kenntnis der Zuckergussbildung an serösen Häuten. Berliner klinische Wochenschrift, 1899, vol. xxxvi. p. 825.

Rosenbach. Eulenberg's Real-Encyclopedie der gesammten Heilkunde, 2te Aufl., 1887, vol. ix. p. 478. Die Krankheiten des Herzens, 1896, p. 129. Die Erkrankungen des Brustfelles. Nothnagel's Specielle Pathologie und Therapie, 1894, vol. xiv. p. 1. Zur Lehre von der Symptomatologie der Pericarditis, namentlich jugendlicher Individuen. Deutsche medicinische Wochenschrift, 1882, pp. 587, 601, 619.

Rumpf. Ueber die Zuckergussleber. Deutsches Archiv für klin. Medicin, 1895, vol. iv. p. 272.

Schmaltz und Weber. Zur Kenntniss der Perihepatitis chronica hyperplastica (Zuckergussleber). Deutsche medicinische Wochenschrift, 1899, vol. xxv. 188.

Schrötter. Die Krankheiten des Herzbutels. Nothnagel's Specielle Pathologie und Therapie, 1894, vol. xv.

Schupfer. Sopra le asciti che si osservano nei malati con sinechia del pericardio. Il Policlinico, 1897, vol. iv. p. 201.

Siegert. Ueber die Zuckergussleber (Curschmann) und die pericarditische Pseudolebercirrhose (Pick). Virchow's Archiv für path. Anatomie, 1898, vol. cliii. p. 251.

Strümpell. Lehrbuch der specielle Pathologie und Therapie, 1890, vol. i. p. 568. A Text book of Medicine, third American edition, 1901, p. 365.

Taylor. On Combined Pleural and Pericardial Adhesions. Lancet, 1898, vol. ii. p. 1109. Polyorromenitis or Combined Serous Inflammations. British Medical Journal, 1900, vol. ii. p. 1693.

Tissier. Calcification du pericarde. Progrès Médical, 1885, vol. xiii. p. 234.

Türk. Beiträge zur Diagnose der Concretio pericardii und der Tricuspidalfehler. Wiener klinische Wochenschrift, 1901, vol. xiv. pp. 860, 914, 927.

van Deen. Een geval van pericarditis chronica gecompliceerd met peritonitis chronica. Nieuw Archief voor binnen- en bintenlandsche geneeskunde in haren geheelen omvang, door Dr. I. van Deen, 1846, vol. ii. p. 1; Schmidt's Jahrbuch, 1847, vol. liv. p. 28.

Variot. Cuirasse calcaire envelloppant le ventricule driot du cœur. Revue de Médecine, 1888, vol. viii. p. 746.

Vierordt. Die einfache chronische Exudative-Peritonitis, 1884. Die Tuberculose der serösen Häute. Zeitschrift für klinische Medicin, 1888, vol. xiii. p. 174.

Villani. Sulla presenza di liquido nella pleura destra nella cirrosi epatica volgare. Riforma medica, 1895, No. 58; Centralblatt für innere Medicin, 1895, vol. xvi. p. 1028.

Wagner. Beiträge zur Pathologie und pathologischen Anatomie de Leber. Deutsches Archiv für klinische Medicin, 1884, vol. xxxiv. p. 536.

Weinberg. Zwei Fälle von Pericarditis tuberculosa mit Herzbeutelverwachung und Ascites. Münchener medicinische Wochenschrift, 1887, vol. xxxiv. pp. 891, 936.

Weiss. Ueber die Verwachsung des Herzens mit dem Herzbeutel. Medicinische Jahrbucher (Wien), 1876, p. 1.

Wells. The Pathology of Active Tuberculosis of the Pericardium. Journal of the American Medical Association, 1901, xxxvi. p. 1451. The Pathology of Healed Fibrous Adhesions of the Pericardium. American Journal of the Medical Sciences, 1902, vol. cxxiii. p. 241.

Werbatus. Ein Beitrag z. perikarditischen Pseudolebercirrhose. Inaug. Diss. Erlangen, 1898.

White. The Cause and Prognosis of Ascites. Guy's Hospital Reports, 1893, vol. xlix. p. 1.

Wilks and Moxon. Lectures on Pathological Anatomy, 1875, p. 371.

NOTE.—Since the foregoing paper was read the following articles have come to hand: Becker: Obliterative Pericarditis, with Hepatic Enlargement and Ascites. Philadelphia Medical Journal, March 25, 1902, vol. ix. p. 485; Simon: Zur Kenntnis der Zuckergussleber. Inaug.-Diss., Königsberg, 1900; Centralblatt für innere Medicin, 1902, vol. xxiii. p. 491; Pfannkuche: Zur Kenntnis der serösen Peritonitis und der Perihepatitis im Zusammenhang mit Perikarditis und Pleuritis. Inaug.-Diss., Kiel, 1901; Centralblatt für innere Medicin., 1902, vol. xxiii. p. 515; Strajesko: Ein Fall von Pseudocirrhose der Leber. Allgemeine Wiener medizinische Zeitung, 1902, vol. xlvii. p. 60; and Nicholls: On a Somewhat Rare Form of Chronic Inflammation of the Serous Membranes (Multiple Progressive Hyaloserositis). Studies from the Royal Victoria Hospital, Montreal, 1902, vol. i. No. 3. The article by Nicholls, which deals especially with the pathologic-anatomic features of chronic inflammation of the serous membrane, is the most exhaustive and comprehensive discussion of the subject that has yet appeared in the English language.

REVIEWS.

AMERICAN EDITION OF NOTHNAGEL'S ENCYCLOPÆDIA OF PRACTICAL MEDICINE. TYPHOID FEVER AND TYPHUS FEVER. By DR. H. CURSCHMANN. Edited, with additions, by WILLIAM OSLER, M.D. Authorized translation from the German, under the editorial supervision of ALFRED STENGEL, M.D. Philadelphia and London: W. B. Saunders & Co., 1901.

THE appearance of the first volume of the authorized American translation of *Nothnagel's Encyclopædia of Practical Medicine* should be hailed with sincere pleasure by the entire profession of this country. The work in the original has long been familiar as a standard authority to those who had access to large libraries, and to them has proved of inestimable value. The publishers have undertaken an enterprise in which they should be supported by all those who are interested in the progress of scientific medicine in this country.

The present volume has been edited with additions by Osler, and it is needless to say that under his supervision the work has assumed a value beyond even that of the original.

The portion of the book devoted to the subject of typhoid fever is naturally much larger than that given to typhus fever, and most of the changes and additions made by the American editor have been to this part of the work. These changes, as stated in the preface, have consisted chiefly in the incorporation within the text of the important results of the investigations by Mallory and Thayer and other American workers.

The consideration of typhoid fever is divided into etiology, pathology, diagnosis, prophylaxis, and treatment. The section on Etiology begins with an admirable historical sketch which represents a type of the progress made in our study and knowledge of disease by modern methods; it is followed by several sections dealing with our knowledge of the nature and properties of the typhoid bacillus, including the subject of infection, and closing with a most apt summary of the conclusions to be drawn from the most recent investigation.

The pathology of the disease, its symptoms and complications, are dealt with at great length. The section on Diagnosis deals with the subject from the point of clinical investigation and from that of bacteriological study. It begins with the statement that "The ideal method of diagnosis of typhoid fever would be the demonstration, with readiness, rapidity, and certainty of its cause, the bacillus of Eberth during every period of the disease," and this statement is undoubtedly true, but as we find emphasized further on, "At present observation at the bedside still retains the first place in diagnosis."

In the section on Prophylaxis we find the topic divided into a discussion of general measures, special individual measures, and preventive

inoculation. Of the latter, it is stated that so far experience is strongly in its favor, although it must stand the test of wider application.

The section on Treatment is very complete. The serum treatment, it is shown, has not as yet proved of much efficacy, and the same may be said of the antiseptic method. The principal factors in the treatment are stated to be the appropriate care and regulation of the condition of the patient, especially in a dietetic direction, and in the treatment of important symptoms, complications, and accidents as they may arise.

Of that portion of the book devoted to typhus fever, the same general statements may be made as regards the first division. The disease has been considered under the same headings and in the same lucid and complete manner that typhoid fever is written of. Typhus fever is so rarely seen by the practitioner that there must be a strong temptation to slur over some of the features of the disease in writing of it. No such lack of care is evident in the present description, and it has the advantage of being written by men who have seen and handled the disease in question.

Particular attention should be directed to the admirable manner in which the work of translating and re-writing has been performed. We have but rarely perused a medical work in which the language was more elegant, or which read with greater ease. We have only to add that should the rest of the volumes prove as excellent in every respect as the one under consideration, the enterprise will be worthy of all possible success. F. A. P.

THE PRINCIPLES AND PRACTICE OF GYNECOLOGY, FOR STUDENTS AND PRACTITIONERS. By E. C. DUDLEY, A.M., M.D., Professor of Gynecology, Southwestern University Medical School; Gynecologist to St. Luke's and Wesley Hospitals, Chicago, etc. Third edition, revised and enlarged, with 474 illustrations, of which 60 are in colors and 22 full-page plates in colors and monochrome. Pp. 761. Philadelphia and New York: Lea Brothers & Co., 1902.

FROM the author's statement in the preface, the reader will infer that, while the original plan of the book has been preserved, radical changes have been made in this edition, and much new matter has been added. One accordingly feels that it is incumbent upon the reviewer to bestow more careful attention upon it than is indicated by the usual perfunctory notice of the latest issue of a successful text-book. Having already presented an extended general review, we shall confine ourselves principally to the new features mentioned by the author. In the new paragraph on the anatomy of menstruation he accepts unhesitatingly Gebhard's view that there is no shedding of surface epithelium during the process. Chapter XV., on Endocervicitis, seems to have received more attention than its relatively slight importance merits. We have always thought that there was no advantage in treating it as a separate disease. Schroeder's operation is so rarely performed at the present time, as compared with amputation of the cervix, that it might well have been omitted. The chapter on Chronic Endometritis has been carefully worked over, especially the section on Curettage, in which there are several excellent new illustrations (Figs. 151 to 156, inclusive). We shall not renew our objection to the author's infective theory, with

which we are not entirely in accord. The present arrangement of the points in differential pathology and diagnosis (which, by the way, is borrowed from Thomas) is a decided improvement here and elsewhere throughout the book. We are a little disappointed to find that chronic metritis is still retained as a separate entity, as it is an "end-process" rather than an inflammatory condition. The explanation that the term is "taken in its broader sense," so as to include even perimetritis, will not render it less objectionable to some more critical readers.

The author manfully champions the cause of cellulitis, and we admire his conservatism even when it leads him to introduce the time-worn parallelism between cellulitis and peritonitis. We shall not enter into a fresh controversy with him regarding the pathology of pelvic inflammation, as his treatment is sound. Chapter XXIII., on the Surgical Treatment of Salpingitis, Ovaritis, and Pelvic Peritonitis, is fully abreast of the times, and shows the author at his best.

The chapters on Fibromyoma and Cancer have been carefully revised and enriched with numerous plates of unusual artistic beauty and practical value (especially VIII. to XIV., inclusive). The author's method of securing the stumps after abdominal hysterectomy, with which we are already familiar, is carefully described and figured—possibly at too much length for a text-book. The same criticism might be applied to the technique of vaginal hysterectomy for cancer. Of the radical abdominal operation he thinks so poorly that he dismisses it with a few lines.

Although it is stated that the chapter on the Pathology of Ovarian Tumors has been rewritten, we still feel that it has not received the attention which its importance warrants. This criticism does not apply, however, to the succeeding chapters on Symptomatology and Differential Diagnosis, and on Ovariotomy. In the latter chapter (XXXIV.) the reader's attention will be at once arrested by the admirable plates (XVII.–XIX.), which are literally in a class by themselves. Tubal pregnancy has been definitely adopted by modern writers as a gynecic rather than an obstetric condition—a surgical fact and not a pathologic curiosity. The author treats it thus, and in the most approved way.

It is unnecessary to repeat our former praise of the chapters on Plastic Surgery. Here, in his descriptions, as in his own work, the author is *facile princeps*. We honor him none the less that among all the changes and innovations of the age he is faithful to his purpose not "to remove the ancient landmarks which the fathers have set up." Doubtless the typical Emmet operation for lacerated cervix will be generally replaced by amputation when any operation seems to be indicated, but it will be long before American gynecologists, of this generation at least, will hold in light esteem the work of that great teacher. Lack of space prevents our noting the changes and additions under the head of Uterine Displacements. We can only say that they seem to render still more readable and instructive these excellent chapters.

After all, Dudley's *Gynecology* needs no fresh encomiums. The best proof of the inherent value of a medical work is afforded by its instant and wide popularity and by the appearance in rapid succession of new editions. Many men would be content to rest on their laurels. Not so our friend the author, who always seeks to give us his best. Surely his hope expressed in the dedication has been realized. He is indeed a "worthy pupil" of his beloved teacher. H. C. C.

BERICHT UEBER DIE VON KOMITEE FUER KREBSFORSCHUNG AM 15 OKTOBER, 1900, ERHOBENE SAMELFORSCHUNG.

REPORT ON THE COLLECTIVE INVESTIGATION MADE BY THE COMMITTEE FOR THE INVESTIGATION OF CANCER. Edited by the Directors, PROFESSORS VON LEYDEN, KIRCHNER, VON HANSEMANN and MEYER, and DR. WUTZDORFF. Supplement to the *Klinisches Jahrbuch*. Jena: Gustav Fischer, 1902.

THE work before us is the first result of a formal attack upon the cancer problem by the medical profession and Government of Germany. Under the initiative of Professor von Leyden a committee was formed in 1900 to foster investigations, and a census of cases under observation on a given day was planned. This was materially furthered by the government, including the Imperial Health Bureau. Cards and directions were sent to more than 25,000 physicians and institutions, and over 12,000 cards available for the census were returned. Although there were many faulty answers, it seems probable that most of the cases known to physicians were reported, so that the material studied forms an imposing mass. While the results to be expected from such an investigation are limited, they cannot but be of interest; and although the tabular form of the report, covering as it does a great array of material, does not lend itself to brief review, it is possible to give some conclusions. It should be said that the present collective investigation is only one of several projects of the committee. Various studies of special topics are now under way. Czerny and Mommsen, for example, are ascertaining the time which elapses after successful operations (on cancer of the breast) before recidive, a period which may have some relation to the latent stage of the primary attack. A number of lectures on certain aspects of cancer have been given in Berlin under the auspices of the committee, but the most promising outcome of its work is the foundation of two institutes for the investigation of cancer—one in Professor von Leyden's clinic, the other in Professor Ehrlich's Institute for Experimental Therapy, in Frankfort. Among the points of interest brought out in the work under review are the following: Cancer generally occurs more frequently in cities than in the country, though there are local exceptions. It is more common in women in cities and in men in the country, also with local exceptions. There are many differences in the morbidity of adjacent places. So in Berlin the proportion is 319 per million; in Charlottenburg, 275; in Rixdorf, 133; in Hamburg, 362; but in Altona, 235. Several industrial towns have very low proportion, as Bochum, with 46 per million. As regards the proportion of women and men, there are many factors, such as age, that have to be still further investigated. Considerable attention was paid to the existence of cancer foci, and some suggestive facts were elicited, but much remains to be discovered. The investigation shows, as has long been known, that cancer is rare in the first two decades of life. The increase begins earlier in women and the decline later. The period of greatest morbidity in women is seventy to eighty years; in men, sixty to seventy years. The latter decade is the only one in which there are more men affected than women. These differences depend on the frequency of cancer in the female breasts and genital organs. Of 1000 cancerous women between fifteen and thirty years of age, the organs mentioned are concerned in 644; between thirty and forty, 746; between seventy and eighty, 374. In men a similar preponderance is

seen on the part of the digestive tract. This part of the investigation contains many details as to the seat that can only be referred to here. A curious fact is that men in cities are more disposed to cancer of the digestive tract than those in the country. Other interesting facts in this connection are the frequency of cancer of the skin in country people and in washer-women, and cancer of the respiratory organs in metal workers. The question whether cancer is increasing is shown by the Prussian statistics to require an affirmative answer. The increase from year to year is so even that accident and error can be excluded. Dr. Wutzdorf has shown in one of the lectures alluded to (*Deutsche med. Wochenschrift*, No. 10, 1902) that the increase of cancer is out of proportion to the increase of population. The idea sometimes advanced that the increase can be explained by the greater average age now reached is not confirmed by figures. On the other hand, cancer shows a tendency to occur earlier than formerly, and is increasing more rapidly in men than in women. The investigation does not tend to prove the idea of the inheritance of cancer in the old and still commonly used sense. Of the men patients, the mothers were affected in 4.3 per cent., the fathers in 4.7 per cent. Of the women, the parents were affected in 7.2 and 3.1 per cent. respectively. As in the case of tuberculosis, there are many examples of a family tendency. Infection was believed to have occurred in 3.6 per cent. of all cases. Two hundred and eighty cases concern husband or wife, 20 the parents, and 135 other people; 5.2 per cent. besides those just mentioned lived with or near other cases of cancer. The report points out that this question is one to which practitioners should pay special attention.

From the details given it may be seen that the report is in many respects a model. In mode of execution the work planned cannot be easily imitated in other countries. But the present report gives large series of figures in connection with many unsettled problems concerning cancer, and points out many lines of investigation that can be taken up in various places. It will therefore be studied with gratitude by all who try to discover the nature of one of the most important diseases that "still baffle the scientific and medical world." The volume includes the report of the Netherlands Commission on Cancer, the results of which correspond closely with the larger ones obtained by the German committee. Three tinted maps show the geographic relations of cancer in general, and in men and women separately. G. D.

AMERICAN EDITION OF NOTHNAGEL'S ENCYCLOPÆDIA. DIPHTHERIA, MEASLES, SCARLET FEVER, AND GERMAN MEASLES. Diphtheria. By WM. P. NORTHRUP, M.D., of New York. Measles, Scarlet Fever, and German Measles. By PROFESSOR DR. TH. VON JURGENSEN, Professor of Medicine in the University of Tubingen. Edited, with additions, by WILLIAM P. NORTHRUP, M.D., Professor of Pediatrics in the University and Bellevue Medical College, New York. Octavo, 672 pages, illustrated, including 24 full-page plates, 3 of them in colors. Philadelphia and London: W. B. Saunders & Co., 1902.

A WORK as well known as Nothnagel's *Encyclopædia* needs no introduction to the medical profession. Its established reputation as a repository of medical knowledge has long since made it an often consulted

work on the shelf of the practitioner. The third volume of the American edition has just appeared.

The first article, on Diphtheria, written by Dr. William P. Northrup, is a masterly exposition of this disease under well classified headings. It is an exhaustive treatise on the subject brought up to date, containing many interesting statistics and numerous instructive charts. The article is concluded by a long and detailed account of the operation of intubation, beginning with an account of O'Dwyer's earliest attempts at this procedure, and gradually tracing the development of the intubation tube up to the most approved pattern as now made. The value of this section is much enhanced by a series of X-ray photographs showing the anatomical relations of the operation.

The remaining articles in this volume by Professor von Jurgensen are preceded by an interesting discussion on the infectious exanthemata in general, which indorses von Kerchensteiner's views regarding quarantine, and propounds a doctrine widely at variance with the board-of-health rules as practised in this country. The admirable article on Measles contains a very thorough consideration of the pathology of this disease, much of its value being derived from a careful study of the Danish records of the Faroe Islands epidemic.

Quite up to the high standing of the preceding chapter is the treatise on Scarlatina, which gives special care to the study of its etiology and pathology, and shows a very just and unbiased weighing of the recorded literature on the subject.

The treatment of Scarlet Fever as advocated will perhaps seem too radical to some practitioners; but we are rapidly passing beyond the belief that the sequential nephritis is due to "catching cold," as formerly taught, or that pneumonia in fever patients is produced by draughts or insufficient bedclothes.

By way of criticism, we might object in some instances to the too liberal translation of some German idioms. But, as the work is not published as an exposition of English rhetoric, the fault is a minor one.

The volume ends with a short consideration of Rubeola and the Fourth Disease. It contains throughout many charts, and has been rendered more valuable to the American reader through appropriate additions by the editor. G. W. N.

REYNOLDS AND NEWELL'S PRACTICAL MIDWIFERY. A Manual of Obstetrics for Students and Physicians. By EDWARD REYNOLDS, M.D., Assistant in Obstetrics, etc., and FRANKLIN S. NEWELL, M.D., Assistant in Obstetrics and Gynecology in Harvard University Medical School, Boston. In one octavo volume of 531 pages, with 253 engravings and 3 full-page colored plates. Philadelphia and New York: Lea Brothers & Co., 1902.

IN their preface the authors assert that any medical book of the present day must needs show reason for its existence. With this view we are in hearty accord, and it gives us great pleasure to be able to say that the present volume meets the requirements of its authors. Naturally, there is nothing new and startling, since in obstetrics, as well as in gynecology, we have reached, as it were, level ground, where—as even the medical societies show—we are all more or less in accord, and where

—for the present at least—the acrimonious discussions of a decade ago are impossible.

But what this book does is to present, in a very clear, practical manner the generally accepted teaching, as modified by the experience of the authors. The work, indeed, bears the unmistakable hall-mark of the authors' practical experience. It is not intended as an exhaustive reference-book, but as a practical treatise for the use of the busy man.

There is much to praise and but little to censure. Of special value are the chapters on delayed labor and on high arrest of the posterior occiput. The section devoted to the consideration of pelvic deformities is also well written and full enough to answer its purpose. The major obstetric procedures receive requisite space, and, in a word, the whole book is well balanced.

To our mind the most important criticism is that the use of rubber gloves is not forcibly advised as a routine measure in delivery. It is certain that no man is justified in attending a woman in childbirth without taking this precaution, if he be at all doubtful of his personal asepsis; and we feel that it is equally certain that the ordinary obstetrician—viz., the general practitioner—can never assume that he is surgically clean.

The only other adverse criticism that we would make is that in the discussion of placenta prævia more space should have been given to the question of diagnosis. W. R. N.

A Text-book of Diseases of the Ear. For Students and Practitioners. By Professor Dr. Adam Politzer, of Vienna. Translated at the personal request of the author, and edited by Milton J. Ballin, Ph.B., M.D., and Clarence L. Heller, M.D. Fourth edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1903.

The publication of a new English edition of this work which stands in a class absolutely by itself as the most complete exposition of the science of otology by its foremost living exponent is a matter of great importance to all physicians especially interested in that subject in this country. It is given to but few books to attain the position of absolute authority which is universally conceded to Professor Politzer's work. Few men have done more than he to bring about the advances in otology which have necessitated the issuance of a new edition of this standard volume. The present edition is larger than the last, and many things which were under dispute at the time that edition was published are now relegated to the position which they should occupy.

A notable feature of the book, and one which is so often lacking from German text-books, is to be found in what one may term its universalism. Not only is the work of German scientists and physicians considered, but due credit is given, *mirabile dictu*, to the work of American otologists such as Knapp, Burnett, Randall, Roosa, and Blake. Most of the work has been entirely rewritten, and all of it thoroughly revised and brought up to date. There are many minor changes in the arrangement, but all of them for the better. Thus the section on otosclerosis, which has replaced that on chronic dry middle-ear catarrh, is entirely recast, and many important results of recent investigation given in an easily accessible form.

Professor Politzer is strongly opposed to operative measures in the treatment of otosclerosis, and thinks we are just as powerless in this condition as we have ever been. The section which deals with operative procedures upon the mastoid process has been enlarged and rewritten, and as it stands now is the most authoritative and up-to-date description of the various methods employed with which we have met.

In no portion of the book do we see greater evidences of scientific advance in otology than in the section which deals with intracranial diseases of otitic origin. It is practically a new section, and it is of the greatest value. Another addition to the work is an appendix containing the prescriptions most commonly used at Professor Politzer's clinic. These prescriptions are, of course, of great value, but their usefulness would be greatly enhanced if they were not written in the metric system. The time has not yet come when the American practitioner can avail himself of this method. It is a pity that the English equivalents were not given in the prescriptions.

The present edition of Politzer is indeed an old friend in a very new dress. The translation is entirely new, having been undertaken by two gentlemen who had been working as voluntary assistants with Professor Politzer for some years, and it is a vast improvement over that used in the previous editions. The typography and the illustrations in the present edition are also much more satisfactory than that of the last. We can only repeat that there is no work in any branch of medicine or surgery which occupies the unique position of Politzer's *Text-book of Diseases of the Ear*. It is an absolute *sine qua non* for the practitioner who devotes special attention to otology or rhinology, and should be in the library of every physician as a book of reference upon these topics. F. R. P.

THE PHYSICIAN'S VISITING LIST FOR 1903 (Lindsay & Blakiston). Philadelphia: P. Blakiston's Son & Co.

THIS *Visiting List* now in its fifty-second year of publication, is one of the most useful books of its class. It presents the usual accompanying letter-press on various matters of practical value to the practitioner, and continues to merit the favor with which it has always been received. R. M. G.

THE MEDICAL NEWS VISITING LIST FOR 1903. Philadelphia and New York: Lea Brothers & Co.

THIS well-known *Visiting List* is published in four different styles: Weekly, dated, for 30 patients; monthly, undated, for 120 patients per month; perpetual, undated, for 30 patients weekly and 60 patients undated.

The arrangement of its record pages is very simple and practicable. The book is strongly made and bound, and contains pages adapted for all the various data which prove of value to the physician in his daily work. It is accompanied by extensive tables of weights and measures, with information of value in various emergencies which may arise, such as poisons and their antidotes, the ligation points for the arteries, how to perform artificial respiration, etc. G. M. C.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

W. S. THAYER, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

Persistent Hereditary Œdema of the Lower Limbs —ROLLESTON (*The Lancet* September 20, 1902, p. 805) has observed a very interesting form of persistent œdema in three members of one family. The mother, aged forty-five years, had suffered from the œdema for thirty-five years. The condition had existed in a daughter, aged sixteen years, since she was thirteen years old. A son, aged thirteen years, had had the œdema since the age of ten.

The œdema was permanent as long as the individual led an ordinary life, became more marked after exercise or a warm bath, but disappeared after rest in bed for some days. In all cases it was only troublesome from the weight and size of the swollen legs. There was evidence of enfeebled circulation in all three cases. In the mother's case pressure on the skin would leave an anæmic area for a much longer time than in normal persons. The boy and girl were both "blue children" at birth and were subject to chilblains, both the feet and hands getting livid by cold. The œdema in all cases was painless. It was permanent, and did not come on suddenly as in angioneurotic œdema. The heart, urine, and blood were normal in all three patients. The only effective treatment was rest for days in the recumbent posture. This relief was only temporary.

Rolleston states that the cases appear to resemble the remarkable family described by Milroy, of Omaha, in which out of 97 individuals in six generations, 22 persons (12 males, 7 females, and three of unknown sex) had solid œdema of one or both legs without any special inconvenience or progressive increase in the disease. In these cases the œdema was congenital, except in one instance, whereas Rolleston's cases were hereditary and developed from the tenth to the thirteenth year. Rolleston states that the disease in some respects resembles both Raynaud's disease and erythromelalgia, but differs

from both in essential features. He suggests that this peculiar œdema from gravitation may depend on some inherent defect or peculiarity of the small bloodvessels, which allows excessive transudation to occur on very slight provocation. The cases are reported to call attention to the occurrence of cases of œdema not due to the usual causes and which are hereditary and may be congenital.

The Presence of the Widal Reaction in Weil's Disease.—ECKARDT (*Münch. med. Wochenschr.*, 1902, xlix. p. 1129) reports two interesting cases of Weil's disease, in each of which the blood serum showed a strong Widal reaction. The first case was that of a young man, aged twenty-two years, whose illness began suddenly with chills, fever, and general prostration. After several days the fever began to diminish, but severe nose-bleeds occurred, while jaundice and an acute hemorrhagic nephritis set in. On the seventh day on entering the hospital the patient appeared very ill and complained of severe pain in the calves; the tongue was dry and coated; the spleen palpable. The patient soon improved subjectively, and the fever disappeared on the following day, but the jaundice and splenic enlargement continued for over two weeks. On the tenth day of the disease the Widal reaction was tried; this resulted in a positive reaction in a quarter of an hour at a dilution of 1/100; in two hours at 1/1000. It was discovered that the room-mate of this patient had passed through a similar illness about a month before. This case was also investigated, the serum showing an agglutination in three-quarters of an hour at 1/50; in an hour and a half at 1/100, and a partial agglutination in two hours and a quarter at 1/1000.

Grünbaum and the author have both noted that the blood of jaundiced individuals has almost always a considerable agglutinative power with cultures of the typhoid bacillus, while the fresh bile, from the same case perhaps, appears to have no such effect. The agglutinative power in the blood serum of these two cases was, however, stronger than has ever been observed in jaundice, while in six other cases it persisted after the jaundice had disappeared. There were also features in the case observed clinically which were not unlike those of an abortive typhoid fever. If the blood serum in jaundice has this agglutinative effect, then, the author suggests, it might well act as a protection to the organism in cases of existing typhoid infection. This naturally brings up the question as to whether Weil's disease may not, after all, be simply typhoid fever which has been aborted as a result of the development of jaundice. Weil, indeed, in his original article states that the disease may be abortive typhoid, while Fiedler, though opposing this theory, admits its possibility. Haas and Weiss have both noted the coincidence of the frequency of Weil's disease at the height of typhoid epidemics.

Eckardt is guarded in his statement and avoids drawing a hasty conclusion, pointing only to the extremely suggestive character of these observations.

Acute Polymyositis.—BACIALLI (*Il Policlinico*, 1902, No. 13, fasc. 1 and 2, 16) reports from Tizzoni's clinic an extremely interesting case of acute polymyositis. The patient was a man, aged thirty-nine years, who, in August, 1899, began to complain of rheumatic pains in the upper part of his trunk,

and especially in the arms, which appeared to be heavy and weak. Eight days later the left arm became swollen, while the general indisposition increased. The swelling soon spread and became diffuse, extending also to the neck, throat, thorax, right arm, and afterward to the legs and feet. These symptoms continued off and on until his entrance into Tizzoni's clinic, in October. At that time the patient was bed-ridden; there was diffuse, subcutaneous œdema, the legs, eyelids, and forehead alone being spared. The mucous membrane of the mouth was greatly injected and œdematous; swallowing was difficult; there was extensive œdema of both upper and lower extremities, of the abdomen, and of the thorax. There was a papular erythema on the back. There was great difficulty in moving the arms and legs. While pressure in the œdematous areas was not painful, yet on deeper palpation severe pain was elicited, clearly due to pressure upon the muscle. The special senses were normal, excepting for slight deafness. The spleen was palpable; nothing remarkable about the reflexes. Reactions to the faradic current were diminished, but elicited by strong currents. The blood showed a slight anæmia; red corpuscles, 3,704,000; hæmoglobin, 75 to 80 per cent.; colorless corpuscles, 5580. The condition remained practically unchanged up to the time of the patient's death. There were at times slight remittent attacks of fever, which rose occasionally to 39½° C., lasting several days. On the 18th of December the patient was suddenly seized with dyspnœa, and died shortly afterward with the phenomena of bulbar asphyxia, due clearly to paralysis of the respiratory muscles. During a febrile period in December a small piece of muscle was removed from the left leg. From the muscle pure cultures of staphylococcus albus were obtained. Similar cocci were seen microscopically in the blood obtained at the point of incision. Pure cultures of the staphylococcus albus were obtained from the heart, liver, and muscle. A centimetre of a twenty-four hours' culture in bouillon injected subcutaneously into a rabbit produced little effect, but a few degrees of fever and no serious impairment of the health of the animal. Microscopically the muscles showed appearances similar to those described by other authors in dermatomyositis. In parts of the muscles there was marked œdema, considerable increase in interstitial connective tissue, with abundant infiltrations of white corpuscles, and here and there extravasations of blood. There were widely distributed inflammatory and degenerative changes in the muscle fibres themselves, of which the author describes three stages:

(1) With considerable increase in the number of the muscle nuclei, while the contractile substance preserved its ordinary structure.

(2) With a light increase in nuclei, while the contractile substance, however, had lost its normal structure, appeared more homogeneous, and was extensively vacuolated.

(3) Where the nuclei, excepting in rare exceptions, were materially diminished in number or have entirely disappeared, while the contractile substance had wholly degenerated into a homogeneous, transparent mass similar to hyaline or waxy material.

These alterations the author attributes to an inflammatory process which has produced in the muscular tissue lesions of various degrees, from simple irritation manifested by a considerable increase in the number of nuclei to much graver lesions, such as degeneration and complete destruction of the

contractile substance. He believes the condition to have been a septico-pyæmia of very gradual course, similar to those which the old authors have called chronic septicæmias.

The muscular lesions are attributed to the effects of toxic products of the staphylococcus albus. The attenuated staphylococcus albus may have entered through the fauces, which from the beginning were markedly affected.

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE UNIVERSITY HOSPITAL,

AND

F. D. PATTERSON, M.D.,

SURGEON TO THE DISPENSARY OF ST. AGNES' HOSPITAL; ASSISTANT SURGEON TO THE DISPENSARY OF THE UNIVERSITY HOSPITAL.

The Treatment of Testicular Ectopy.—COUDRAY (*Revue de Orthopédie*, January, 1902), after a careful review of the subject, states, in conclusion: 1. The treatment of testicular ectopy—ectopy without hernia—should be commenced early, at the age of two or three years. 2. Before attempting mechanical treatment one should try the thyroid treatment, with a dose of 5 centigrammes a day for those under the age of three, and 10 centigrammes daily for those who are over that age, and the dose in the latter class progressively increased to 15 or 20 centigrammes daily. 3. If two or three months of this treatment gives no appreciable results, then one should have recourse to mechanical reduction by pressure or traction. This should be done for four or five minutes each day. 4. When the testicle is distinctly beneath the ring and the cord slips easily along one should advise the carrying of a bandage like a fork, which has the effect not only of retaining the testicle beneath the external ring, but also prevents the wall guarding the ring against the issue of intestine. This wall is often very feeble in these cases. Experience has shown that the unilateral bandage cannot be well applied in the case of young children. It may be preferable in those cases of unilateral malposition, and this may also apply to the hernia of young children, but the double bandage is to be preferred, as a rule, as it has much more firmness. It is well to wear this bandage two or three years, renewing it whenever necessary. The fixation of the testicle at the bottom of the sac may be a useless manœuvre. The bloodless method has the greatest chance of success in young children and those up to the age of ten or twelve years. In those who are older it seems that its employment favors the development of hernia or hydrocele of the cord. 5. Surgical interference is indicated in those cases where there has been some check in the preceding methods; that is to say, when the cord cannot be drawn out or when the testicle is painful

or uncomfortable. In the cases of inguinal ectopy, one nearly always pulls the testicle out in those children who are well nourished. In the iliac variety, on the contrary, when the testicle is not mobile, it is to be hoped that surgical intervention will permit of its replacement in a normal position. In spite of this, the search for the iliac testicle, when painful, is indicated, and it should be removed if replacement is impossible, for a large number of cases have demonstrated that this retention is a source of danger. In all cases one may do a radical cure; that is to say, the resection of the vagino-peritoneal canal after ligation of the neck of the sac in the abdomen. 6. In those children who are not under proper surveillance, and who, in consequence, benefit but vaguely by a bandage, the indications are for early operation. 7. One question remains, Are the testicles which are brought down by the bloodless method less exposed to the danger of atrophy than those replaced by operation? Possibly, but the demonstration of the fact still remains to be made.

Resection of Nearly Eight Feet of Gangrenous Intestine; Recovery.—HARRIS (*Medical Record*, New York, October 11, 1902) states that the removal of large portions of the intestines, with recovery of the patient, is becoming much more common than in former years, and where there is an abundance of time in which to prepare the patient, with plenty of assistance and good light, this operation is robbed of many of its difficulties; but when, on the other hand, the operation is performed in an emergency, after the patient has been brought a long distance in an ambulance, he being more or less exhausted, with a violent peritonitis in progress, it is an entirely different thing. These circumstances, together with the extreme length of the intestine removed and the apparent complete recovery of the patient, are the reasons for reporting the case of a man, aged thirty-three years, whose history was negative except for four attacks of severe abdominal pain during the past five years. The present attack came on suddenly in the morning with severe pain, which centred in the umbilical region. This soon passed off under brandy and massage of the abdomen, and the patient laid down and slept about an hour. On arising the pain began again, and was more severe than at first. A physician was called and two hypodermics, each of one-quarter grain of morphine sulphate, were given without relief. The patient vomited fluid and mucus, and enematas of hot water proved ineffectual. There was a point of tenderness about the size of the palm of the hand above and to the left of the umbilicus. Operation being decided upon, the patient was removed to the hospital in an ambulance, a distance of twelve miles, and arrived there at 1.30 o'clock in the morning. Nothing definite was learned by an examination of the abdomen, and an incision was then made in the right hypochondrium. As soon as the abdomen was opened there was a tremendous gush of blood-stained serum containing blood and lymph, showing that an acute peritonitis was in progress. Exploration with the fingers showed a large mass of intestine, bound down in the right iliac region, so the wound was closed and the abdomen reopened in the median line, when a very large mass of gangrenous intestines appeared. The mass was about seven inches in the transverse diameter, and the coils of which it was composed ran, for the

most part, transversely, a few, however, were parallel with the long diameter of the abdomen. The point of constriction was close to the posterior abdominal wall and the cæcum. It being impossible to uncoil the intestines, the constricting band, which seemed to be mesentery of about the size of a lead pencil, was divided and the intestines spread out on hot towels and allowed to remain for over twenty minutes. The intestine proved to be the ileum; the mesentery in many places was sloughing and entirely gone. There was one spot where a perforation had taken place, but there did not seem to have been much extravasation. The color not having improved, the ileum was clamped and divided close to the cæcum, the remaining vessels of the mesentery were tied and cut away close to the spine; above, the division was made one inch from the upper limit of the gangrene. The mass of gangrenous intestines was then removed, and the abdomen thoroughly flushed out with hot salt solution, and preparation made for joining the intestines. The opening in the cæcum was closed, the edges being inserted and closed with a double row of Lembert sutures, one-half of a Murphy button being first put into the cæcum. This button was then pushed against the wall on the other side of the cæcum beside the appendix, and, an opening being made, the button was brought through and held by an assistant. The end of the ileum was inverted and closed by a double row of Lembert sutures, the second half of the button having been previously placed in the bowel. This was brought through in the same way as the other, and the intestine was joined to the cæcum by a lateral anastomosis. No additional sutures were required except in the mesentery. The abdomen was again thoroughly flushed out, the wound closed in the usual manner, and a wet bichloride dressing applied. The portion of intestine removed measured seven feet ten inches. The patient had two large abscesses in the abdominal wounds during convalescence, one at the first incision and the other at the opening in the median line. These finally closed and the patient left the hospital weighing more than when he entered, and now feels as strong as ever. The Murphy button was found in the rectum on the twenty-fourth day, and removed. In closing, the author gives a list of thirty-five cases in which the length of the resected portion of intestine varies from forty inches in the first case to twelve feet two inches in the last.

Operation for Paralytic Club-foot.—SCHANZ (*Centralblatt für Chir.*, June 28, 1902), states that paralytic club-foot is usually treated at the present day by first undertaking the correction of the deformity, and then trying, through transplantation of the tendon, to increase the lost function of the peronei. In transplanting one usually secures the best material by incising off a portion of the tendo Achilles. The bloody part of this treatment is really two separate operations—transplantation and lengthening of the tendo Achilles. While both of these operations may be performed at one sitting, as a general rule it will be found better to first do the transplantation, and then, some four or five weeks later, proceed to lengthen the tendon. The reasons for this are: 1. The same reasons as apply to the operation in two sittings on the congenital cases. 2. The outward turned sole comes into position better. 3. The simple condition of the wound when transplantation

only is performed, for experience has shown that the transplanted portion remains free from the rest of the tendo Achilles sooner if both are maintained in full extension. After the first operation the foot is in the "pointed foot" position. This is not a disadvantage, for one can then place the new Achillo-peroneal tendon shorter, and through this obtain better transplantation. In addition, one is then in a position to judge accurately just how much the end of the foot must be corrected in order to produce the best functional result. In these cases there is almost always some shortening of the affected leg, which is equalized by allowing a certain degree of the "pointed foot" portion to remain, and then compensating by a high-heeled shoe. In many cases the operation of lengthening is then not required. The author's experience with this method of treatment has been in every way most satisfactory, while operation at one sitting proved a partial failure in the two cases in which it was tried. The result was about half of what it should have been—the "pointed foot" position was there, but the anterior portion of the foot was in adduction, and the heel did not become more prominent upward and backward, as is the case in a good result.

The Use of Argyrol in the Treatment of Acute Gonorrhœa.—SWINBURNE (*Medical Record*, New York, October 11, 1902) states that argyrol comes in dark-brown scales, is very hygroscopic, and is soluble to almost any degree in water. The solutions keep well without deteriorating. It contains nearly 30 per cent. of silver. It possesses one drawback, and that is its staining properties. On account of this it has to be very carefully used, for though when treated with boiling water the stains are readily removed, yet it is distinctly disagreeable to the patient to get it on his underwear. The author has treated with this drug at a dispensary upward of 350 cases having gonococci. In the beginning the patients were given a single daily injection of 2½ to 3 drachms of a 1 per cent. solution, which was held by the patient for ten minutes in the anterior urethra. Cases in which the posterior urethra was involved received in addition a deep instillation of an ounce of the solution through a small flexible catheter, which was then withdrawn and the solution urinated out. Those cases that came regularly recovered completely in a moderately short time. After these injections there was absolutely no reaction and no pain.

In private practice the author uses several methods according to different circumstances, such as the severity of the disease, the chance of aborting the disease and the patient's ability to come frequently or not. Treatment may be daily, and in such cases irrigation with one quart of hot 1 to 1000 or 1 to 2000 solution of argyrol, followed by a 2 or 5 per cent. injection or instillation, as the case demands, with the patient's use of a 2 per cent. solution at home, once or twice a day in addition, or it may be no injections are used by the patient at home. Some patients may only be able to come once or twice a week—they get the same treatment when they come to the office, and use a 2 per cent. solution two or three times a day at home. In chronic cases good results follow the use of this drug. Cases needing sounds get now, as a lubricant on the sound, a 5 per cent. ointment, made with adeps lanæ as a base, the argyrol being rubbed up with water just enough to

render it smooth before incorporating it with the ointment. Too great stress cannot be laid on the painlessness of the drug. A 10 per cent. solution dropped in the eye hardly produces a sensation of warmth. To sum up, this drug has decided gonococcidal powers; it has a decided effect in reducing and allaying the inflammation of the disease; it can be used safely in almost any strength and at any stage of the disease; the injection can be repeated almost as frequently as the fancy of the physician dictates; the author has not seen any unpleasant symptoms due to the use of the drug and believes it to be one of the most valuable remedies given to the profession in recent years.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

PROFESSOR OF MEDICINE AND THERAPEUTICS AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; VISITING PHYSICIAN TO ST. MARK'S HOSPITAL,

AND

SMITH ELY JELLIFFE, M.D., PH.D.,

PROFESSOR OF PHARMACOGNOSY AT THE COLLEGE OF PHARMACY; CLINICAL ASSISTANT AT THE VANDERBILT CLINIC (COLUMBIA UNIVERSITY), NEW YORK.

Antagonism of Morphine and Cocaine and the Employment of Cocaine in Morphine-poisoning.—DR. EDWARD T. REICHERT, in a lengthy contribution on this subject, concludes as follows: 1. That the antagonistic actions between morphine and cocaine are of a powerful and widespread character, extending to almost every function involved, and are, therefore of such a character as to justify the conclusion that one may be regarded as meeting the important indications of a successful antagonist to the other. 2. That the only important synergistic actions are as excitomotors and their tendencies in some individuals to cause syncope. 3. That cocaine is not only sufficiently powerful to successfully antagonize the profound depressant actions of morphine upon general metabolism and body temperature, but as a whole is more powerful, both relatively and absolutely, in morphinized than in normal dogs. 4. That the increase in heat production caused by cocaine is due in part to a direct excitation of general metabolic activity, chiefly by motor excitement; and that even in the absence of muscular excitement cocaine may fully counteract the morphine depression. 5. That the effects caused by a given dose of cocaine per unit of body-weight vary in intensity within wide limits. 6. That the changes in body temperature following the injection of cocaine are, with few exceptions, closely related quantitatively and qualitatively to the changes in general metabolism, and are, therefore, a fairly reliable index of the intensity of the cocaine actions —in other words, of the extent to which the cocaine is counteracting or superseding the depressant actions of morphine. 7. That the temperature coefficients in normal and morphinized dogs after cocaine are practically

identical, showing that morphine does not exert any specific actions on heat dissipation which interfere with the typical temperature-raising action of the cocaine. 8. That the typical cocaine effects may be delayed in the morphinized animal, and then appear with marked intensity, as shown by the increase of heat production, body temperature, and by motor excitation at a time when in normal animals they are lessening rapidly. Under such conditions the dangers of morphine-poisoning may be superseded by those of cocaine-poisoning. 9. That owing to a coexistent paralytic-convulsant state in the morphinized animal the administration of cocaine or other powerful excitomotor may develop or intensify the convulsant moiety, and thus render a non-lethal dose of the morphine lethal, or hasten death when the dose is lethal. In man the convulsant element is almost without exception so unimportant that there is probably little or no danger of this kind except after unnecessarily large doses of the excitomotor, or in exceptional individuals in whom the excitomotor action of the morphine is marked. 10. That the value of cocaine in morphine-poisoning probably depends chiefly upon the extent to which it antagonizes the depressant actions of morphine upon general metabolism and body temperature. 11. That the power of cocaine as a respiratory stimulant depends almost solely upon its action upon the heat mechanism. 12. That owing to the tendency of cocaine to cause syncope in certain individuals, to its excitomotor action, to the marked variability in the intensity of the effects caused by a given dose per kilo to the body-weight, to the occasional delay or latency in the typical actions of cocaine in morphinized animals, and to the fact of the greater value of small to moderate doses in morphinized dogs, it should be administered in morphine poisoning in man in small doses cautiously repeated.—*Therapeutic Gazette*, 1902, vol. xxvi., pp. 462, 518.

Camphor and the Morphine Disease.—Dr. J. Hofmann says that in healthy persons it has been demonstrated that camphor is a strong heart muscle stimulant, and that it causes an increase of blood pressure. In the initial action of morphine a directly reverse action takes place, whereas in the *habitué* stimulation is the usual result. When the morphine is withdrawn from the fiend, dilatation of the heart, with fluttering, takes place; this disappears on resuming the alkaloid. The author claims that this cardiac sensation is a vital one for the well feeling of the individual, and he believes that camphor used at such a time enables the patient to regain this sense of equilibrium. He details the history of a patient, a physician, who kept an accurate record of his sensations, for whom he recommended decreasing doses, by hypodermic injection, of morphine, and slightly increasing doses of camphor by the mouth on the advent of the patient's "abstinence" symptoms. Full tables of the progress of the case are given. Validol (a valeric acid menthol ester) was used as an adjuvant to the camphor.—*Therapeutische Monatshefte*, 1902, vol. xvi., p.360.

A Fake Morphine Cure.—Dr. O. Emmerich reports on a new cure for morphine that has appeared in the European market. Inasmuch as it has come to America, its composition as determined by the author and others should be known. It is termed "antimorphine," and is advertised as a

new remedy containing no morphine, and useful for the treatment of patients at home, "without a doctor." He found that the remedy contained large quantities of morphine, and his analysis was confirmed by the chemists of a large manufacturing house. They reported that the remedy contained 1.4 per cent. of anhydrous morphine, or the equivalent of the hydrochloride of 1.84 per cent.—*Deutsche medicinische Wochenschrift*, 1902, vol. xxviii., p. 584.

Arsenic in the Treatment of Phthisis.—Dr. H. Cybulski has been using sodium arsenate in the treatment of phthisis, with good results. He administers it hypodermically, in the following solution: Sodium arsenate, 3 grains; carbolic acid (½ per cent.), 5 drachms; 1½ minims is to be injected at one time once per diem, at body temperature. This dose is doubled every second day until 15 minims are reached. In his work, which has now extended over a number of years, as a rule twenty injections were used serially. If improvement were noted, two to three weeks were permitted to elapse and the injections renewed. The signs of improvement were increased in the body-weight and appetite, reduction of temperature, and diminution of the night-sweats. The intestinal symptoms were not affected. Diarrhœa, an uncomfortable accompaniment of arsenical medication when given by the mouth, was absent. The subjective conditions were helped. The effect of the drug on the lungs is *nil*, he thinks.—*Münchener medicinische Wochenschrift*, 1902, vol. xlix., p. 1393.

The Diphtheria Serum Question.—Professor Kassowitz returns to this subject in a second paper, in which he reiterates his former claims, and endeavors by means of charts and statistical studies to maintain his position that the diphtheria serum is of little if any service.—*Therapeutische Monatshefte*, 1902, vol. xvi., p. 499.

A Case of Poisoning from Pennyroyal.—Dr. G. W. Holland reports a case of poisoning from this drug. The patient, a married woman, aged twenty-four years, was very desirous of avoiding pregnancy, and having gone a week beyond her usual period without any appearance of the menstrual flow, applied for a prescription to "bring on the flow." Oil of pennyroyal was prescribed. At 3 o'clock in the afternoon she took seven drops, without result. The dose was repeated at 6 o'clock, with no better success. At 9 o'clock, just before retiring, she swallowed about half a teaspoonful, and soon after fell asleep. She awoke in about an hour, complaining of great dizziness and nausea. Shortly after she vomited and complained of cramps and stiffness of the extremities. She lost consciousness, and was seized with violent tonic contraction of all the muscles, opisthotonos being well marked. The spasm lasted only a few minutes, and after incoherent talking and tossing for about half an hour the toxic symptoms began to subside, and consciousness was regained. On the arrival of the physician she complained of great weakness, cramps in the stomach, and a slight desire to go to stool. The pulse was 108 and feeble. Respiration and pupils were normal, and as the toxic symptoms were subsiding the author gave nothing, and merely watched the course of the symptoms. The following morning the patient

was able to attend to her regular duties. The desired effect of bringing on the flow was not accomplished. The toxic dose in this case was half a drachm, and from the symptoms which were produced it is evident that the drug should be administered with great caution.—*Virginia Medical Semi-Monthly*, 1902; vol. vii., p. 319.

Treatment of Typhoid Fever.—Dr. Francois Bouchard gives the results of a detailed study of intestinal antisepsis in the treatment of typhoid fever after the method of Teissier. In 1890 this author described his method as follows: (1) Morning and evening a capsule of naphthol, 7 grains, and 4 grains of bismuth salicylate; (2) four cold enemata a day, to encourage diuresis; (3) following the afternoon enema, an enema of 1 drachm of extract of cinchona and 15 grains of quinine sulphate, dissolved in an infusion of valerian; this is used as antithermic and tonic; (4) the diet is liquid—a little milk, ten ounces of white wine, broths, etc. As a result of this method in 151 patients treated during twelve years the statistics showed a mortality of 4.63 per 100. He believes that the temperature, the abdominal and digestive symptoms, and the general condition are all much improved. Convalescence is shorter, and complications, particularly the intestinal complications, are much rarer. The effects of the treatment commence to show only on the fourth day.—*Thèse de Lyon*, 1902, No. 177.

Impermeability of the Lung for Ammonia.—Dr. R. Magnus determined to test the permeability of the lung for this gas. By intravenous injection minute doses of ammonia cause the most intense irritation of respiration, convulsions, and disturbances of circulation and of the central nervous system. The statement of Knoll that in tracheotomized and vagotomized animals the long-continued inhalation of ammonia is harmless, seems, in the light of these facts, so astonishing that the following test was made: Tracheotomy was performed on a rabbit after the vagi had been cut, and the animal allowed to inhale air saturated with ammonia. No constitutional symptoms, only local irritation of the mucous membranes followed, while if sulphuretted hydrogen was substituted for the ammonia, death occurred in fifteen seconds. The experiment was then modified so that ammonia was injected into the veins and the expired air passed into Nessler's reagent, yet in no instance was a precipitate obtained, despite the fact that the blood, on autopsy, had a bright-red color and smelt strongly of ammonia. The experiment was then repeated by injecting directly into the pulmonary artery, with the same result. If, however, artificial respiration were kept up after death, the reagent soon became cloudy. The experiments showed that the impermeability is a property of the living tissues.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlviii., p. 100.

Affinity of Carbonic Oxide for Hæmoglobin.—Dr. G. Huffner says that if hæmoglobin is exposed to a mixture of carbonic oxide and oxygen it will combine with both gases; but since the affinity of the substance for carbonic oxide is much greater than for oxygen, even small amounts of the former present in the atmosphere will render a large percentage of the blood unfit for oxygenation. He has constructed a table of percentages,

from which it is evident that with but 0.05 per cent. of carbonic oxide in the air as much as 27 per cent. of the hæmoglobin present is seized upon by the poisonous gas.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlviii., p. 87.

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,
OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Laparotomy for Adherent Retroflexion during Pregnancy.—DOLERIS (*La Gynécologie*, June, 1902) treats this condition by opening the abdomen, separating adhesions, and shortening the round ligaments. He reports a successful case in which the patient, who was in the third month of pregnancy at the time of the operation, was delivered easily at full term, the uterus remaining in its normal position after involution had occurred.

Lymphangiectasis of the Vulva.—DURET (*Journal des Sciences Méd. de Lille*, 1902, No. 5) believes that there is a form of this disease which is due to streptococcus infection as well as to filaria. The superficial variety affects principally the external genitals and lower limbs, and is usually accompanied by œdema and elephantiasis of the skin; small vesicles appear, which may open spontaneously, causing a copious discharge of lymph, which may be so profuse as to lead to profound anæmia, which, however, yields to constitutional treatment.

Premature Menopause.—ADDINSELL (*British Medical Journal*, May 17, 1902) reports the case of a young woman, aged twenty-six years, whose menstruation had been entirely normal up to the time of her marriage. During the wedding journey she was under great excitement at the time when her monthly flow was due. It had never appeared since. When examined six years later she was in good health, although she suffered from flushes of heat, which occurred every few weeks. Her uterus had undergone senile atrophy, the sound entering to the depth of an inch. The ovaries were apparently normal. The patient stated that her sexual desires were preserved, and that her breasts sometimes became swollen and tender.

Structure of the Senile Uterus.—VERRONI (*Annali di Ostetricia et di Ginecologia*, 1901, No. 7) presents the results of his studies of twenty-eight normal uteri removed from women between the ages of sixty and ninety-two. In most of the specimens the mucous and submucous layers had undergone atrophy, together with the glands; in others, the submucous layer was

thickened and the glands were actually hypertrophied. The capillaries were numerous and tortuous, and many groups of leucocytes and infarcts were observed. In general, the epithelium of the cervical canal was well preserved and the glands cystic.

The smooth muscular fibres were present, without marked degeneration, but with an excess of fibrous tissue. Vacuoles, infarcts, and collections of leucocytes were scattered throughout the muscular layer. The bloodvessels were intact, the capillaries being often visible to the naked eye. While the endothelium of the larger vessels presented a normal appearance, there was marked hypertrophy of the tunica, with frequent calcareous degeneration. The writer believes that the anatomy of senile uteri proves that the condition is the result of normal involution, and not of an inflammatory process.

Sterilization of Phthisical Women.—NEUMANN (*Centralblatt für Gynäkologie*, 1902, No. 12) criticises Pincus' plan of abolishing the risk of pregnancy in phthisical subjects by destroying the endometrium by atmokausis. The writer prefers resection of the tubes for several reasons, psychical and physiological, as menstruation is preserved and the patients are spared the mental and physical disturbances of the menopause. His operation, which is safe and easy, consists in excising a wedge from each tube and suturing the ends without disturbing the ovaries.

Intra-abdominal Pressure.—KOSSMANN (*Centralblatt für Gynäkologie*, 1902, No. 27) replies to a former article of Meyer, who denies the existence of a true intra-abdominal pressure. While agreeing with the latter in his assertion that this pressure is constantly changing and that it is never negative, he denies that it varies at every point in the cavity. The writer claims that this pressure is everywhere alike, and is only unequal when gas or fluid is abnormally present in the free cavity. Intra-abdominal pressure becomes a disturbing factor, he believes, when it is sufficient to overcome the normal power of resistance of the muscular wall.

Perforation of the Uterus.—SCHULZE-VELLINGHAUSEN (*Centralblatt für Gynäkologie*, 1902, No. 27) reports two cases of accidental perforation of the non-pregnant uterus with the sound, in both of which the organ was subsequently extirpated and was carefully examined microscopically. The writer concludes that not only do atrophy, tuberculosis and malignant disease of the uterus favor accidental perforation of the non-puerperal uterus, but also degenerative changes in the muscular wall. The accident is by no means uncommon, and great care should be observed in deciding these cases medico-legally, especially when the question of undue violence or want of skill is brought up.

[The question naturally suggests itself: Why was it necessary to remove the uterus in the two cases reported? The accident is seldom followed by any serious results under aseptic conditions.—ED.]

The Paravaginal Incision in Hysterectomy.—SCHAUTA (*Monatsschrift fur Geb. u. Gyn.*, Band XV., Heft 2) is not enthusiastic over the radical

abdominal operation for cancer of the uterus, since in two of his patients who succumbed to the operation neither the glands which were extirpated nor those which remained were diseased. It has not yet been satisfactorily demonstrated that cases in which cancerous glands have been removed remain free from recurrence. Any comparison between the conditions in the pelvis and axilla is unjustifiable. Most stress should be placed upon the removal of the cancerous foci that are nearest to the uterus, and this is accomplished by Schuchardt's paravaginal method, which the writer has practised in thirty cases, with five operative deaths. Some of these were inoperable by other methods; in fact, his proportion of operable cases has risen from 15 to 46.5 per cent. In the cases reported the bladder was wounded four times, the uterus three, and the rectum once. If the pelvic lymph glands are affected the operation is to be regarded as simply palliative.

[No comment is necessary, except to call attention to the writer's own statistics and his admission with regard to the cases selected for operation. —ED.]

Tuberculosis of the Appendix and Adnexa.—KRAUS (*Centralblatt für Gynäkologie*, 1902, No. 27) reports a case in which a nullipara, aged thirty years, gave a history of appendicitis ten years previously. A tumor was discovered in Douglas' cul-de-sac, which, at the operation, proved to be an enlarged ovary and a tubercular tube and appendix. An interesting point was the fact that the tubercles were confined to the mucous membrane of the distal end of the tube and to the adherent tip of the appendix. The reporter concludes that the process began in the appendix and extended outward to the Fallopian tube, possibly along the appendiculo-ovarian ligament. The ovary was the seat of an abscess, but no tubercles could be found, nor were tubercle-bacilli observed in any of the sections.

The Malignancy of Solid Embryomata.—JUNG (*Centralblatt für Gynäkologie*, 1902, No. 15) affirms that solid and cystic embryomata present no essential points of difference. The former, as well as the latter, are to be regarded as benign in character and are parasites rather than true neoplasms.

He reports two cases. In the first the cystic element predominated. The solid portion contained not only the usual epidermal structures, but nerve tissue, cartilage, bones, and numerous pouches lined with columnar epithelium and surrounded by smooth muscle fibres. The peritoneum and omentum were studded with grayish nodules, and the retro-peritoneal glands were enlarged as high up as the transverse colon, but no trace of sarcomatous degeneration was found microscopically. The nodules proved to be not metastases, but simply obliterated vessels. The patient was in good health a year and a half after the operation and had gained twenty pounds.

In the second tumor all three embryonic layers were represented, the connective tissue being so rich in cells that malignancy was suspected; but the subsequent history of the patient proved the contrary.

The writer calls attention to the fact that twelve of the twenty cases of teratoma recorded are described as being either undoubted sarcoma or sarcomatous in appearance. Cancerous degeneration of these growths has not

hitherto been described, though he thinks that it might occur. Only one genuine case of retroperitoneal metastasis of a teratoma has been reported by Ewald, which is a strong argument against its malignant character. The prognosis is accordingly good, and the tumor should always be removed.

Abscess of the Uterus.—FRANQUÉ (*Sammlung klin. Vorträge*, No. 316) bases his paper on this subject on twenty-eight doubtful and fifteen clear cases collected from the literature. The condition is due to puerperal sepsis, and may terminate by perforation of the uterus and general peritonitis, or the patient may recover, with atrophy and obliteration of the organ. Repeated chills and elevation of temperature, associated with prolonged discharges of pus, enlarged and tender uterus, should point to the probable condition. The diagnosis is difficult, however, since a suppurating sarcoma or fibromyoma may be easily mistaken for it, even when it follows labor. The prognosis is most unfavorable, the mortality without operation being 75 per cent. Incision and drainage of the abscess through the cervical canal is dangerous; it is advisable only when the abscess has ruptured into the uterine cavity. In chronic cases vaginal extirpation of the uterus may be performed, but the abdominal route is preferable. If the abscess is small and localized and the adnexa are healthy, it may be possible to attach the uterus to the abdominal wound, incise, and drain, but abdominal hysterectomy will usually be necessary.

Menopause.—KLEINWACHTER (*Centralblatt für Gynäkologie*, 1902, No. 20) presents some personal observations based on 373 cases. Assuming that the normal menopause occurs between the ages of forty-five and fifty years, he found that in 130 women the climacteric atrophy of the internal genitals was present too early. In 40 menstruation did not cease until after fifty years; 13 were fertile at 45 years and over. Senile endometritis was noted in 7 cases. In 4 women between the ages of fifty-eight and seventy-one years, who had always enjoyed good health since the menopause, metrorrhagia appeared, due, the writer inferred, to calcification of the uterine vessels since no other cause could be assigned.

Artificial Distention of the Bladder.—DESGUIN (*Journ. de Chir. et Ann. de la Soc. Belge de Chir.; Centralblatt für Gynäkologie*, 1902, No. 23) recommends that in cases of prolapsus the bladder should be distended to its utmost capacity before beginning an anterior colporrhaphy or vaginal hysterectomy, in order that the organ may be lifted out of the pelvis. He injects from two to two and one-half pints of boric acid solution.

Fibromyoma of the Urethra.—LÖRMBERG (*Upsala Läkareförenings Förhandlingar; Centralblatt fur Gynäkologie*, 1902, No. 34) has collected twenty-seven cases from the literature, to which he adds the following: The patient, aged thirty-one years, was admitted to the hospital on account of hemorrhage from the urethra without other symptoms. On examination a tumor the size of a hazelnut was seen in the dilated urethral opening; it was eroded, quite sensitive, and bled easily. The growth was easily shelled out of its capsule.

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE; PROFESSOR OF OBSTETRICS AND DISEASES OF INFANCY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE WOMAN'S MEDICAL COLLEGE; VISITING OBSTETRICIAN TO THE PHILADELPHIA HOSPITAL, ETC.

Pubiotomy.—At a meeting of the Netherland Gynecological Society, VAN DE VELD (*Centralblatt für Gynäkologie*, 1902, No. 4) reported the case of a woman, aged twenty-eight years, in her second labor. Her first child was premature and perished soon after birth. The patient had been in labor twenty-four hours and had a rapid, feeble pulse, while the contraction ring in the uterus was plainly formed and the head had not yet entered the pelvis. The internal antero-posterior diameter was 8½ cm. The heart sounds were good.

On account of the presence of the contraction ring, version was declined. Because the child was living, craniotomy was also declined, while Cæsarean section was not attempted because the pulse of the mother was high and the amniotic liquid was foul. The operator chose pubiotomy, because the wound through the ramus of the pubes would be less easily infected than the open pubic joint. The operation proceeded successfully, and a living child was born. On the third day the mother had a mild attack of thrombosis on the left side where the incision was made. On the eighteenth day the patient was convalescent.

Rupture of the Uterus Through Cicatricial Tissue.—In the *Centralblatt für Gynäkologie*, 1902, No. 4, PEHAM reports the case of a patient in her fourth pregnancy who had a justo-minor pelvis. Her history showed that the first confinement proceeded naturally, and that in the second labor the patient was brought to the hospital with complete rupture of the uterus. The intestine prolapsed through the uterine tear. The laceration began 1 cm. above the anterior lip of the cervix and extended considerably toward the right side and above. The intestine was replaced by the insertion of the hand into the uterus, iodoform gauze was carried through the rent into the abdominal cavity, and the lower uterine segment and vagina were packed with sterile gauze. The patient made a good recovery and was discharged, about three weeks after her admission, in good condition. Two years later the patient again became pregnant and had an abortion at about seven months. She recovered without accident.

She was again admitted to the hospital in active labor near full term. She complained that a few hours previous she had experienced a sudden and severe pain as if something in the abdomen had suddenly torn. Labor pains stopped, and a physician who was summoned sent her to the hospital.

Upon examination her temperature was slightly subnormal, her pulse 90,

and she gave little evidence of rupture of the uterus. The uterine muscle was not firmly contracted, there was no hemorrhage, the head of the child was movable above the pelvis, and no heart sounds or fœtal movements could be obtained. On vaginal examination a laceration was found on the right side, the upper end of which could not be reached from below. The cervix admitted three fingers without difficulty, the membranes had ruptured, and the head was movable above the pelvic brim. There was a discharge of dark-colored blood from the genital organs. The pelvis was considerably contracted, and delivery was accomplished by craniotomy. This was followed by no hemorrhage, but by a considerable failure in the pulse. On vaginal examination a rupture of the uterus was easily found, and through the rupture the umbilical cord led to the placenta, which had escaped into the abdominal cavity. The abdomen was opened as soon as possible, and the placenta found slightly adherent to a portion of the omentum. Hysterectomy was immediately performed, with the removal of the uterine appendages. The patient made an uninterrupted recovery. On examining the uterus its contractile portion was found very strongly developed, but the remainder of the womb was deficient in strength and elasticity.

A second and similar case also reported is that of a patient in her second labor who had a flat rachitic pelvis. The patient was admitted to the hospital with normal pulse and temperature, the child well developed and the head above the brim of the pelvis. The membranes were unruptured, but labor had not proceeded. After the patient had been under observation for some time, and it was seen that she could not deliver herself, version was performed under anæsthesia, and the child was extracted. It was somewhat asphyxiated, but revived. The placenta was spontaneously expelled, and the uterus contracted well. An abnormal bleeding continued from the womb, and, upon examination, rupture of the uterus was found extending through the right side of the lower uterine segment to the peritoneal tissue above.

The treatment consisted of irrigation of the womb with lysol, and packing with iodoform gauze. Cold applications were placed over the abdomen, and tincture of opium was given. The patient made a good recovery.

When the history of her first labor was obtained it was found that version had been performed, followed by an unusually difficult extraction, and that a laceration had then occurred through the same tissues, following the version and extraction.

The third case was a patient in her third labor with contracted pelvis, at whose first confinement three years previously it was necessary to incise the cervix to perform craniotomy. At her next labor she was delivered of a child by breech presentation, and had fever during her convalescence.

In her present illness she had received a severe injury by straining and falling, and considerable amniotic liquid had escaped. This happened four days before admission, and the patient had a chill the night previous. On admission she was greatly weakened, and on examination the fœtus was found in transverse position. Upon vaginal examination the scar was found upon the right side of the cervix, extending through the entire cervix and somewhat above. Similar scars were also present in other portions of the cervix. The membranes had ruptured and the thigh of the child could

be felt within the uterus. The heart sounds were loud and strong, and as dilatation proceeded the right arm could be detected. The cervix was incised and version was performed with extraction, the scars being incised as the extraction proceeded to avoid serious injury. The extraction of the arms was so difficult that the child died during this manipulation, and craniotomy was performed upon the aftercoming head. Upon examination a tear was found through the lower uterine segment upon the right side, extending to the peritoneum. The patient was treated by gauze packing as in the other cases and made a tedious recovery. Her illness was complicated by facial erysipelas and by parametritis upon the right side of the pelvis.

[The writer gives no reason for choosing the method of delivery employed in preference to that by abdominal incision. It seems to us that a considerably contracted pelvis, with the history of rupture of the uterus in former labor and with the presence in two of the cases of a living child, justified delivery by abdominal incision. The selection of version in a case where rupture of the uterus had formerly occurred seems inexplicable.]

Vaginal Use of Elastic Bags.—VOIGT (*Archiv für Gynäkologie*, 1902, Band lxvi., Heft 1) reports from the clinic in Dresden the vaginal use of elastic bags during labor in 510 cases among 12,445 labors. This was practised under antiseptic precautions, the bags being carefully cleaned by soap and water, by bichloride of mercury, and the vagina douched with bichloride of mercury before the bag was inserted. Three indications were recognized as justifying this practice: The necessity for retaining the amniotic liquid when premature rupture of the membranes occurs or is threatened, the dilatation of the soft parts, and the stimulation of uterine contractions. The last indication is regarded as questionable, and Voigt believes that ordinarily elastic bags should not be used for this purpose.

In cases of contracted pelvis spontaneous labor seemed to be stimulated by this procedure, although pelvic contraction is not a valid indication for the use of the bag. In cases where the pelvis is slightly flattened where version is determined upon, and where the operator wishes to retain the amniotic liquid as long as possible, this method has decided advantage. In a highly-contracted pelvis, through which a child cannot be delivered alive, it would not only do no good, but positive harm.

In cases of deep attachment of the placenta and placenta prævia this method is inferior to the use of the tampon of antiseptic gauze. In eclampsia where labor is advanced sufficiently to make delivery possible in a short time these bags were of use in dilating the soft parts for labor.

In some cases where labor must be hastened in the interests of the child this method was of use, as it increased the uterine contractions and dilated the vagina and pelvic floor. In some cases it was seen to be useless, as cicatricial contraction or rigidity was so great as to prevent the good result from the method.

The pains must have already begun to make this method of value, and there must be no cicatricial contraction of the cervix, which must be dilated to admit one or two fingers; the bag should be moderately filled only when it gives but little discomfort to patients and does not prevent sleep between the pains. Its use does not influence the puerperal period unfavorably, but

hastens convalescence by preventing exhaustion. In the interests of the child it shortens labor, and thus lessens the danger of fœtal death.

Urobilinuria during Pregnancy as a Sign of Fœtal Death.—In the *Annali di Ostetricia*, 1902, No. 4, MERLETTI reports a series of investigations to determine the presence of urobilinuria in pregnancy and to what extent it increases at the death of the fœtus. He found that it exists in most cases of pregnancy, and that it gradually but considerably increases in the event of fœtal death.

Quintuplets.—In the *Sei-I-Kwai Medical Journal*, 1902, No. 3, vol. xxi., SATO reports a case of multiple birth with five fœtuses.

The mother was a multipara, aged thirty-seven years. She married at fifteen years, and had borne a number of children, with easy parturition. There was an heredity of multiple conception on the side of her father's family. The last menstruation appeared in April, and parturition took place at about the eighth month of pregnancy. Her physicians were not summoned until she was in active labor, when it was learned that she had experienced considerable inconvenience during pregnancy through excessive size and general dropsy, well marked in the lower extremities. She worked as usual until a few days before parturition. She had supernumerary nipples. Labor proceeded spontaneously. The first child, a boy, was delivered, covered with the membranes; four minutes afterward the second child, a girl, was delivered; five minutes later the third child, a boy, was born, followed by a common placenta for the first and second children; after another five minutes the fourth child, a girl, was delivered by the feet, and another placenta for the third and fourth children was expelled. It was then supposed that all of the children had been delivered.

On examining the abdomen a fœtal head was felt above the navel, and upon gentle pressure the fifth child, a boy, was brought down and delivered. A single placenta for the fifth child was shortly afterward discharged. There was a moderate hemorrhage, which ceased upon tamponing and compressing the uterus.

The first placenta weighed 666 grammes, the second 685 grammes, and the third 277 grammes. The weight of the children varied from 1111 grammes to 1555 grammes. The children were inferior in development, and soon succumbed.

The Estimation of the Transverse Diameter of the Pelvis in the Parturient Woman.—SANDSTEIN (*Journal of Obstetrics of the British Empire* October, 1902) contributes a paper in which he gives the results of his measurements of the pelvis to obtain the transverse diameter in the parturient woman. After a thorough study of various sorts of pelves he comes to the conclusion that for practical purposes the transverse diameter of the pelvic brim is to be estimated in any pelvis by simply dividing the intercristal diameter by two. This very simple method will enable the obstetrician, from external measurements, to deduce the important measurements desired internally.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,

OF PHILADELPHIA.

Rapid Development of a Fibrosarcoma of the Tonsil.—At a meeting of the Chicago Laryngological and Climatological Association, April 21, 1902 (*Journal of the American Medical Association*, May 24, 1902), DR. CHARLES M. ROBERTSON narrated the case of a farmer, aged sixty-two years, who acquired an extensive fibrosarcoma of the tonsil and soft palate, which began in a small swelling above the left tonsil a few days after that organ had been pricked with a straw in use for picking the teeth. By the end of eight weeks it had developed into a large tumor occupying the left palatal arch, well down to its base, involving the tonsil and the side of the pharynx as far as the epiglottis, and up behind the edge of the hard palate as far as the left Eustachian tube. It extended forward into the mouth to within one inch of the incisor teeth. The following week the growth was removed under chloroform anæsthesia, and was found to be encapsulated. Twenty months had passed without recurrence.

Œdematous Laryngitis.—DR. F. E. ROSS, of Erie, Pa., reports the following case (*American Medicine*, May 24, 1902) in an habitual drunkard, aged forty-three years, complaining in great distress of inability to talk or swallow, found to be due to an œdematous uvula as large as a man's thumb, and which was relieved by scarification. Three hours later Dr. Ross was summoned to a saloon, where he found the same man suffering with intense dyspnœa, for which he opened the trachea with a tenotome from his pocket case, and kept the wound patulous with a pair of uterine forceps. The patient was taken to a hospital and a tracheal tube inserted. Although the dyspnœa was relieved, the œdema progressed so that by the evening of the first day the whole anterior and lateral cervical regions were enormously distended, the effusion extending down over the clavicles on to the chest. At the end of the first day it began to subside, and on the third day the tube could be removed. The patient left the hospital upon the eleventh day. As to etiology, the œdema was believed to be of nephritic origin.

Adenoma of the Nose, with Incipient Sarcomatous Metamorphosis: Removal by External Access.—DR. EMIL MAYER, of New York, reports (*American Medicine*, August 2, 1902) a case of an Irishman, aged sixty-eight years, who had suffered for twenty years, subsequent to a kick from a horse, depressing his nose and producing obstruction to his breathing. During the six years previous to his being sent to Dr. Mayer his physician had removed numbers of polypi, with some relief; but during the last year the character of the growth had so changed that he suspected sarcoma and advised radical

procedure. Dr. Mayer found the left side of the nose deformed, with a large tumor on the left occluding both nasal passages. The entire hard palate was depressed and the presenting tumor soft and yielding, the growth extending into the posterior nares, and the slightest touch produced hemorrhage.

The nose was cut through on the left and drawn aside with retractors, revealing an immense growth, which was thoroughly evulsed with forceps and curette. "It was found that the whole mass had originated from the left middle turbinated bone, and this place was thoroughly cauterized. There was entire absence of the vomer, the nasal bones on the left, and of most of the superior maxilla that formed the hard palate. The cartilaginous septum was not affected, while the bones had become entirely absorbed. There was no evidence, however, of involvement of the bone so far as the growth was concerned; hence no part of the superior maxilla was removed. The patient made an excellent recovery." The examination of the tumor showed it to be formed mainly of papilliform adenomatous tissue, the balance consisting of small myxomatous polypi.

Phlegmonous Laryngitis.—At the meeting of the Chicago Laryngological and Climatological Association, April 21, 1902 (*Journal of the American Medical Association*, May 24, 1902), Dr. O. T. Freer read the history of a "Case of Phlegmonous Laryngitis Terminating in Abscess in Front of the Larynx," in a man, aged fifty-four years, who had never been ill before. It suddenly began in the night in a glossitis, attendant with dyspnœa and tumefaction around the larynx, with gradually increasing stenosis, which necessitated tracheotomy on the tenth day, and it was forty days before the canula could be dispensed with.

Supernumerary Uvula.—Dr. Joseph Mullen, of Houston, Texas, depicts (*Laryngoscope*, May, 1902) a case of this anomaly in a male negro, twenty-five years of age, well developed and in apparent good health.

Fatal Membranous Glossitis.—At the meeting of the Toronto Clinical Society, May 7, 1902 (*Journal of the American Medical Association*, May 24, 1902), Dr. A. J. Harrington reported an unusual case of membranous glossitis, of which he stated he could find no trace in the literature. The specimen was presented. The condition occurred in an infant, aged eleven months—a fine, healthy, robust child. It had measles in March, 1902. On April 8th the whole cast of the tongue exfoliated, and the system of the child was thoroughly saturated with sepsis. The child died the following morning.

A Durham Tube in the Right Bronchus.—Dr. E. D. Ferguson, of Troy, reports (*American Medicine*, February 1, 1902) a case in which the outer canula of a Durham tracheotomy tube had fallen into the right bronchus, owing to lack of the collar at the distal extremity in front of the shield. After an extensive incision of the trachea, nearly to the bifurcation, the missing canula could be felt by the finger in the right bronchus, and its upper edge was seen by reflected light from a head mirror, so that it was

promptly removed with forceps. The patient, a woman, aged forty-two years, made an excellent recovery.

The Chemical Pathology of the Saliva and of the Pharyngeal Secretions as a Means of Diagnosis.—A paper on this subject was read by DR. D. BRADEN KYLE, of Philadelphia, before the Twenty-fourth Annual Congress of the American Laryngological Association (*American Medicine*, July 12, 1902). Examination of the salivary reaction by the use of litmus paper in the mouth is practised more or less frequently in attending to buccal, oral, and pharyngeal diseases, but special chemical investigation of the constituents of the secretions is rarely practised. In the paper before us the writer refers to his own observations commencing in 1895–96, and also to those of the dentists Michaels, of Paris, and Kirk, of Philadelphia; and he believes that a good many throat and nasal affections, reflex and otherwise, could probably be traced in origin to perverted salivary secretion.

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

AND

MILTON B. HARTZELL, M.D.,

INSTRUCTOR IN DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

The Occurrence of Bullæ in Lichen Planus.—WHITFIELD (*British Journal of Dermatology*, May, 1902) reports the case of a single woman, twenty-seven years old, in whom an extensive eruption of lichen planus was accompanied by vesicles and bullæ upon the legs and feet. A histological examination of the fluid found in the bullæ showed a small number of leucocytes, of which about 20 per cent. were eosinophile and the remainder polynuclear. There were also a few staphylococci and streptococci present. As to the relation of arsenical treatment to the occurrence of this unusual complication, the author found that out of seventeen reported cases nine had not taken arsenic before the appearance of the bullæ. In most cases the bullæ corresponded exactly with the papular lesions. No constant blood alteration, such as eosinophilia, etc., was present.

A Case of Hyphomycetic Granuloma of the Skin.—SCHAMBERG (*Journal of Cutaneous and Genito-Urinary Diseases*, September, 1902) reports the following interesting and unusual case: A woman, aged forty years, had upon the right forearm two large patches elevated a half-centimetre or more above the surrounding skin, having a mammillated surface almost papillomatous in character; they were of a dull red color, firm to the touch, and quite tender.

A few days after coming under observation a pustule developed a short distance from one of the patches, which rapidly increased in size, ruptured, and became a small, rapidly growing tumor of granulation tissue. From time to time other pustules appeared which followed the same course. Under applications of acetanilid and a weak solution of permanganate of potash marked improvement took place. Microscopic examination of sections showed a fungus consisting of mycelial threads staining with gentian violet scattered throughout the cell-infiltration in the corium. Culture and inoculation experiments were negative. As the author was not certain of the trichophytic nature of the fungus he preferred to report the case as a hyphomycetic granuloma.

Primary Actinomycosis of the Occiput.—BOHM (*Archiv für Dermatologie und Syphilis*, Bd. lix., Heft 3) reports a case of primary actinomycosis occurring in the occipital region. The patient, a butcher, twenty-six years old, had an acute inflammatory swelling, accompanied by fever and pain. Under treatment with ice-bags and solution of acetate of lead the inflammatory symptoms subsided, but the swelling remained. After a time scattered, firm nodules appeared in the swollen parts, which slowly underwent softening, forming abscesses which opened spontaneously. In the fluid evacuated from these abscesses were yellowish-gray granules, which were found by microscopic examination to contain the actinomyces fungus. After dividing the fistulæ, pure tincture of iodine was injected, which produced marked improvement, so that after two months' treatment, during which about twenty-five injections were made, the disease was cured. No recurrences have taken place in three years. The author thinks infection occurred through scratching the scalp with the fingers, which had been soiled by handling the flesh of an actinomycotic bullock or hog.

Psoriasis following Nervous Shock.—BALZER and FAURE-BEAULIEU (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 6) at a recent meeting of the Société Française de Dermatologie et de Syphiligraphe reported the case of a man, aged fifty-four years, who, after seeing one of his children narrowly escape being run over by a tram-car, was seized with nervous trembling, chills, and fever so severe as to confine him to bed. The next day red spots were noticed upon the left forearm which were followed in a day or two by others upon the chest and legs. Fifteen days later, upon his admission to the hospital, he presented a typical guttate psoriasis. The patient had never had any cutaneous affection previous to this attack of psoriasis, nor was psoriasis present in any member of his family.

A Case of Dermatitis Verrucosa Probably Caused by the Bacillus Coli Communis.—ANTHONY (*Journal of Cutaneous and Genito-Urinary Diseases*, August, 1902), under the above title reports a case in which a lesion clinically resembling tuberculosis verrucosa cutis followed a burn with muriatic acid. At the base of the thumb was a patch of vegetating papillæ surrounded by a red zone one centimetre wide, in which were numerous small abscesses from which a drop of pus could be evacuated by pressure; pus could also be squeezed from the apices of many of the papillæ. Blastomycosis, tubercu-

losis verrucosa cutis, and streptococcic dermatitis were excluded. With ordinary stains a short bacillus was found in the pus which was fully identified as the colon bacillus. Examination of sections showed an enormous proliferation of the epithelium of the epidermis. Here and there were formations resembling, in a slight degree, the so-called epithelial pearls found in cancer of the skin, but these were not at all typical. Small abscesses were also present which were filled with polynuclear leucocytes.

The Treatment of Lupus Vulgaris by Applications of Radium.—HALLOPEAU and GADAUD (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 71), at a séance of the Société Française de Dermatologie et de Syphiligraphie, presented a patient with a verrucose lupus vulgaris of the hand which had been much improved by applications of radium. The first application was made during seventy-two hours, and produced a lasting discoloration; fifteen days later ulceration followed. Two months later another application of radium was made, lasting one hundred and twenty hours; this produced a loss of substance which still persisted. Seven other applications were made of twenty-four hours' duration; these left no trace. Compared with the condition presented during former visits to the hospital, the improvement was very considerable. The verrucous elevations had disappeared, leaving a smooth cicatrix of healthy aspect.

Upon the same occasion (*Ibid.*) Danlos reported four cases treated in the same manner, and expressed the opinion that there was a great future for radium in dermatotherapy. Its employment was justifiable in erythematous lupus and lupus vulgaris, in hypertrichosis, superficial cancers, nævi, etc.

Psoriasis following Vaccination.—DORE (*British Journal of Dermatology*, September, 1902), at a meeting of the London Dermatological Society, presented three patients in whom a more or less extensive psoriasis appeared after vaccination. The first patient was a young man, aged twenty years, without any history of a previous skin affection. On the eighth day after a revaccination a red, scaly eruption appeared upon the legs, which soon extended to the arms and trunk. Upon appearing at the hospital he presented an extensive psoriasis, which differed from an ordinary attack only in the fact that the site of the vaccination was marked by circular, red, scaly patches. The second case occurred in a woman, aged thirty years. The vaccination did not heal for two months, and eventually became covered with red, scaly patches, which were followed by others on various parts of the body. When seen she had typical psoriasis. The patient was otherwise healthy, and had not had any skin affection previously. The third case was a young woman, aged eighteen years, in whom, after vaccination, a "red, patchy rash" appeared which, disappearing in three days, was followed by psoriasis presenting the usual features. In this case there was a history of an eruption at eleven years of age resembling the present one.

Noma and Hospital Gangrene.—MATZENAUER (*Archiv fur Dermatologie und Syphilis*, Band lx. Heft 3) in a recent paper attempts to prove that, clinically as well as bacteriologically, noma and hospital gangrene are identical processes. From a study of the literature of the affection it is evident that

noma occasionally occurs epidemically; and the circumstance that numbers of cases quickly follow one another in institutions proves that it is transferred from one patient to another. It always develops where there are already defects in the mucous membrane. Clinically there is no definite dividing line between noma and hospital gangrene; they are both an inflammatory process which early leads to coagulation necrosis of the tissues. The bacilli found in noma agree in form, size, and tinctorial characteristics with those in hospital gangrene. The author concludes that, since clinically no definite line can be drawn between these two affections, and since the histological and bacteriological findings are the same, noma can only be regarded as a form of hospital gangrene.

An Anomalous Superficial Dermatitis Occurring during Typhoid Fever and Having Some Resemblance to Psoriasis Rupioides.—ROLLESTON and MERCER (*British Journal of Dermatology*, June, 1902) report the case of a married woman, aged twenty-eight years, with a typical attack of pronounced typhoid fever, in whom, besides the ordinary typhoid roseola upon the abdomen, there was an eruption of peculiar round and oval lesions resembling the early stage of seborrhœic eczema. These rapidly increased in size and number, there being about twenty small round circles and oval areas of varying sizes. The lesions began as erythematous macules, slightly rough to the touch, and scarcely raised above the surface. A greasy, brownish-gray or greenish scale formed on this erythematous base resembling closely a flat limpet in shape. Upon the flattened apices of several of these scales there were yellowish, cheesy nodules, but no distinct pustulation. The scales after a time separated spontaneously, the skin beneath being normal in the centre, but presenting an erythematous margin which gradually broadened and faded, in this way producing confluent rings. The eruption was practically limited to the lower part of the chest and front of the abdomen. Bacteriological examination showed the staphylococcus albus, but no typhoid bacilli nor any fungus.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,
OF DENVER,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,
PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

Etiology of High Myopia.—GUTTMANN, Breslau (Graefe's *Archiv. of Oph.*, 54, ii.), analyzes ten years' clinical material in Professor Magnus' polyclinic. Of 49,200 patients—48.9 per cent. males, 51.1 per cent. females—3688 were affected with myopia of both eyes (anisometropia excluded),

equalling 7.5 per cent., a proportion not greatly different from that of other Continental clinics. Of these, 57 per cent. occurred in males and 43 per cent. in females, confirming previous statistics as to the greater liability of the male sex to myopia.

Of high degrees, 6 D. and upward, there were in round numbers 1000—27 per cent. of the total number of myopes and 2.1 per cent. of the entire clinical material. A striking result comes out from the study of these 1000 cases as regards the proportion of the sexes affected with high myopia, viz., 36 per cent. in males and 64 per cent. in females, almost the direct opposite of the proportional distribution of low myopia. It appears that high myopia is about twice as prevalent in the female as in the male sex. This striking excess admits of but one explanation, viz., that such myopias, not dependent upon close work, are largely cases of essential myopia, to which the female sex shows a special predisposition.

From a further analysis the author concludes that three-fourths of all cases of myopia of high degrees are instances of essential myopia, and but one-fourth is found in subjects who have been engaged from an early age at very close work—occupational myopia. The latter form is about equally prevalent in both sexes, whereas the female sex is more than twice as liable to essential myopia. Of high myopias in men one-third are dependent upon close work, and but one-fifth in women. Occupational myopia of 10 D. and over is much rarer than essential myopia equally high. Complications of the fundus occur in 28 per cent. of high myopia. Accordingly the female sex is more than twice as predisposed as the male. Of the complications the most frequent is lesion of the macula. Detachment of the retina is rare. High essential myopia is more likely to be attended with complications than similar degrees of occupational myopia.

In over two-thirds of all instances of high myopia, essential and occupational, no hereditary influence can be traced.

A Study of the Sense of Sight Shortly after Operations Successfully Performed on Adults for Congenital Blindness.—KOENIGSBERG, Orenburg (translated from the Russian by Carrick in the *Scot. Med. and Surg. Journ.*, July, 1902), made a study of what was actually recognized by the sight alone in three subjects successfully operated for congenital cataract at the ages of sixteen, eighteen, and twenty-eight years, respectively. In each case the most familiar objects could not be recognized until they had been touched. After they had been learned by the sight, sight alone was adequate for their subsequent recognition. The appreciation of space and distance was only attained after prolonged practice. On the other hand, objects were seen from the first as they are, and not reversed in spite of their being so imaged upon the retina. When a cylinder with concentric bands of different colors was shown, the patients at once named the respective positions of the bands. On asking the subject of the experiment to touch the upper part of the cylinder the hand was quickly stretched to that point, and the same test was employed in defining the lower part of the cylinder and with a like result.

The Nerve Supply of the Lacrymal Gland.—PARSONS (*Royal London Hospital Reports*, May, 1902) reviews the anatomical, histological, embryo-

logical, physiological, and pathological evidence of, and records some further observations upon, the nerve supply of the lacrymal gland. It has generally been considered that the secretory nerve fibres to the gland are derived from the fifth nerve. Some observers, reasoning principally from analogy with the salivary gland, have included the cervical sympathetic as an additional source of supply. More recently the seventh has been alleged to be the secretory nerve, and not the fifth. The writer inclines to this view, while admitting that the question is not yet settled.

Sympathetic Inflammation Affecting the Posterior Part of the Uveal Tract.—FISHER (*Royal London Ophthalmic Hospital Reports*, May, 1902) refers to two main classes of sympathetic ophthalmia. Of these iridocyclitis forms by far the larger; the other constitute but a small fraction. The latter are invariably called cases of neuroretinitis or papilloretinitis.

The prognosis in these cases is much better than in inflammations of the anterior uvea. Fisher thinks that it is the posterior uveal tract and not the nerve and retina which is primarily affected. In this condition the chorio capillaries might still retain a sufficiently free circulation to allow the retina which it helps to nourish to regain its full function, which is hardly to be expected in true inflammation of that structure. He reports a case.

Treatment of Incipient Cataract by Collyria and Ocular Baths of Iodine.—BADAL (*Journ. de Med. de Bordeaux*, No. 29, 1901) has used collyria of sodium or potassium iodide in the strength of 1 : 250 for the collyria and 1 : 40 for the baths in incipient cataract; one or two drops of the collyria to be dropped into the eye morning and evening; the baths to be used twice a day in an eye cup. He has never seen any cataract become retrograde as a result of the treatment; but he affirms that in certain cases development has been arrested, and in a still larger number the progress has been unusually slow.

Treatment of Diphtheritic Conjunctivitis by the Instillation of Antitoxin into the Conjunctival Sac.—CHESNEAU (*Gazette Med. de Nantes*, February 15, 1902) reports upon the instillation of Roux's serum, every two hours in two drop-doses, into the palpebral fissure, in alternation with lemon juice. Eleven children, between the ages of fifteen months and two years, were so treated, with the most satisfactory results. Upon the second, or at latest the third day, the swelling of the lids went down, the folds in the skin reappeared, and the false membrane was reproduced only in spots. In four or five days the disease had become simply a common catarrhal conjunctivitis, which rapidly recovered. Of prime importance was the absence of corneal complications in this series of cases.

Tuberculous Dacryoadenitis and Conjunctivitis.—STIEREN, of Pittsburg, Pa. (*Johns Hopkins Hospital Bulletin*, November, 1901), reports a case of tuberculosis of the lacrymal gland and ocular conjunctiva, with a review of the literature—twelve other reported cases.

Notwithstanding the great prevalence of tuberculosis, the eye enjoys greater freedom from tuberculous invasion than any other part or organ.

This immunity is due to the fact that the eye is almost constantly exposed to a lower degree of temperature than that in which the tubercle bacillus thrives, is very often exposed to the direct sunlight, is constantly bathed in and flushed by the tears, and expulsion of germs from the conjunctival sac is aided by the movements of the lids. The epithelial structure of the exposed parts of the eye, resting on a basement membrane, affords very little opportunity for invasion and growth.

The case reported occurred in a colored girl affected with general tuberculosis. The growth disappeared almost entirely without surgical intervention, this having been refused. The discharge and curettings were examined for tubercle bacilli, but always with a negative result.

The author's conclusions are:

1. Tuberculosis of the conjunctiva may be either ectogenous or entogenous; tuberculosis of the lacrymal gland must be hematogenous.

2. The presence of the tubercle bacillus in tuberculous conjunctivitis and tuberculous dacryoadenitis is not a *sine qua non* of the diseases.

3. Tuberculous conjunctivitis and dacryoadenitis may undergo cure. Surgical intervention is indicated only after therapeutic and proper hygienic measures fail.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.,

ASSISTANT PROFESSOR OF HYGIENE, HARVARD MEDICAL SCHOOL,

AND

EDWARD F. WILLOUGHBY, M.D.,

OF LONDON, ENG.

Causation of Beriberi.—In the July number of this JOURNAL (p. 84) were given certain facts pointing to decorticated (white) rice as a cause of beriberi. Additional evidence that the disease is of alimentary origin is given by DR. ARTHUR STANLEY (*Journal of Hygiene*, July 1, 1902, p. 369), who shows that, in Shanghai, the Chinese prisoners under municipal police supervision are attacked more extensively than is the general public. The incidence in four widely separated prisons, completely isolated in every respect, was of approximately the same degree, but greatest where the length of incarceration was most prolonged, namely, at the jail. None of the European or Indian staff at these places was affected, although they resided in the same compound. This excludes soil and immediate surroundings as a cause. The fact that the disease occurs mainly among natives aggregated for periods longer than one month favors the idea of its propagation by contagion. Again, the operation of the infective agent, whether conveyed in food, or by parasites or by contagion, would be favored by aggregation of potentially infective units. The food supply of

three of the four prisons was from different sources, but the rice in use at all four was found to be of poor quality, weevilly, and mouldy. A change was made in the rice at all the prisons; an excellent quality of Annam rice was procured at an increased price. From the beginning of August the new rice was given out every three days. Toward the end of September, the number of cases diminished markedly, and in October they ceased. In spite of this fact, and because of a to-be-expected seasonal diminution, Stanley says the "results of the rice experiments were, therefore, probably negative," which finding would suggest that whoever chose that particular time for experimentation had not all of the qualifications of a true scientific investigator.

Stanley, in spite of an evident disinclination to believe in the rice theory, mentions the following facts, which certainly support it: In Japanese prisons beriberi has become a rarity since the daily allowance of rice was changed to a mixture of barley and rice in the proportion of 6:4. In 1899, the prisoners at Nugata were fed on Chinese rice, and from January to March, 400 of their number (1000) had beriberi. Those supplied with white (decorticated) rice were affected more extensively than those supplied with red rice. In Corea, where the Japanese and Coreans live side by side, the former eat rice and have the disease, and the latter live chiefly on peas, without rice, and escape. In the Straits Settlements, the Tamils decorticate their rice after it is cooked, and have very few cases of beriberi; while the Chinese and Malays eat rice that has been husked a year or longer, and suffer extensively.

From a series of sixteen conclusions with which Stanley's paper terminates the following may be quoted as having a bearing on the theory of alimentary origin:

6. Inasmuch as, apart from rice, the food supply of three out of the four prisons was from different sources, and a change of rice for all the prisons to one of recognized good quality produced no well-marked effect on the prevalence of the disease in two months, food infection would appear not to be a factor in the cause.

7. Beriberi being a peripheral neuritis, which is a pathological condition usually associated with toxæmia, food would, in the absence of a primary lesion (as in diphtheria), seem specially indicated as a cause. For the same reason the cause would be met with in specifically contaminated food rather than in either qualitative or quantitative changes in diet.

8. The marked and apparently primary degenerative action of beriberi on heart muscle, like that produced by diphtheria, and to a less degree by influenza and alcohol and arsenic poisoning, all of which may also cause peripheral neuritis, and the remarkable clinical resemblance of beriberi to diphtheria in the frequency of death from sudden heart failure, would also indicate a form of chronic poisoning.

9. The identity of the pathological changes in beriberi, diphtheria, and arsenic and alcohol poisoning, and the grouping of alcoholic poisoning with ergotism, pellagra, and lathyrism, which are caused by poisons produced by parasites in vegetable foods, suggest the possibility of the cause of beriberi being a toxin derived from an extraneous parasite of some article of food.

11. The oft-repeated statement that a beriberi patient recovers quickly when removed to a fresh locality may not indicate that this disease is a place infection, but rather that the source of the toxin may be removed by change of residence.

13. Something more is required for the prevention of beriberi than attention to the general rules of sanitation, such as ventilation, cleanliness, and diet. Moreover, isolation of cases as they arise, followed by disinfection, does not suffice to limit the disease.

14. The maximum incidence of beriberi in Shanghai being at the end of the tropical summer (the remainder of the year being quite temperate), the liability to recurrence yearly at this season in the same patient would be compatible with the elaboration of a toxin favored in its origin by the period of maximum atmospheric heat and moisture.

The Presence and Vitality of Bacteria in Oils.—Dr. Baldas (*Gironale della Reale Soc. Italiana d'Igiene*, February, 1901) notes that while surgeons are careful to secure the complete sterilization of all the water they use in the performance and subsequent treatment of operations, the possibility of oils and fats applied as vehicles of drugs to the absorbent and denuded surfaces of wounds and burns or to mucous membranes being the means of introducing septic or even pathogenic microbes does not appear to have been thought of. Dr. Baldas, impressed by the fact that the tubercle bacillus, and more often pseudotuberculous bacilli, had been detected in butter, began by examining the fats and oils most used in commerce and freely exposed to contamination from the air, and next those used in medicine and surgery. He found in these many of the hyphomyceti, of which the penicillium glaucum was the most frequent; the schizomyceti occurred more rarely, and he failed to discover any pathogenic germs in the crude oils. But as their absence in the samples in question was no proof that they might not be introduced, he proceeded to the experimental sowing of the oils with various pathogenic bacteria. When the oils were heated to considerable temperatures the germs rapidly disappeared, but at ordinary temperatures they retained their vitality unimpaired for two months, the duration of his observations. He did not employ the B. anthracis on account of its exceptional vitality, but he found that the B. coli, Eberth's bacillus, and the staphylococcus aureus and albus lost none of their vitality and virulence.

Notice to Contributors.—All communications intended for insertion in the Original Department of this Journal are received only *with the distinct understanding that they are contributed exclusively to this Journal.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this Journal, will be translated at its expense.

Liberal compensation is made for articles used. A limited number of reprints in pamphlet form will, if desired, be furnished to authors in lieu of compensation *provided the request for them be written on the manuscript.*

All communications should be addressed to

Dr. Francis R. Packard, 1831 Chestnut Street, Philadelphia, U. S. A.